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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Feb 24	PCTGEN now available on STN
NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	SEP 09	CA/CAPLUS records now contain indexing from 1907 to the present
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation
NEWS 38	AUG 18	Simultaneous left and right truncation added to ANABSTR

10/ 068,114

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 07:36:56 ON 11 SEP 2003

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DICTIONARY FILE UPDATES: 9 SEP 2003 HIGHEST RN 582289-61-0

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STN Note 27, Searching Properties
in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

Uploading 10068114.str

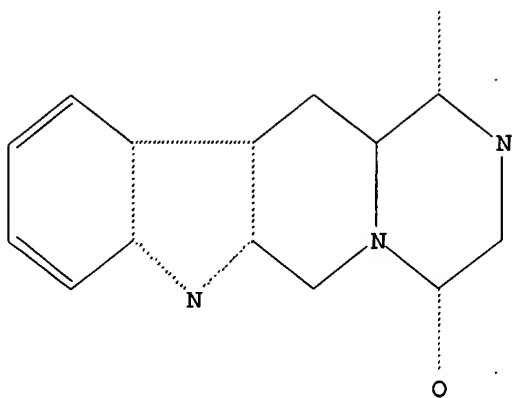
L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

10/ 068,114



Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful

FULL SEARCH INITIATED 07:37:25 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 292 TO ITERATE

100.0% PROCESSED 292 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

L2 0 SEA SSS FUL L1

=> s octahydropyrazino

L3 21 OCTAHYDROPYRAZINO

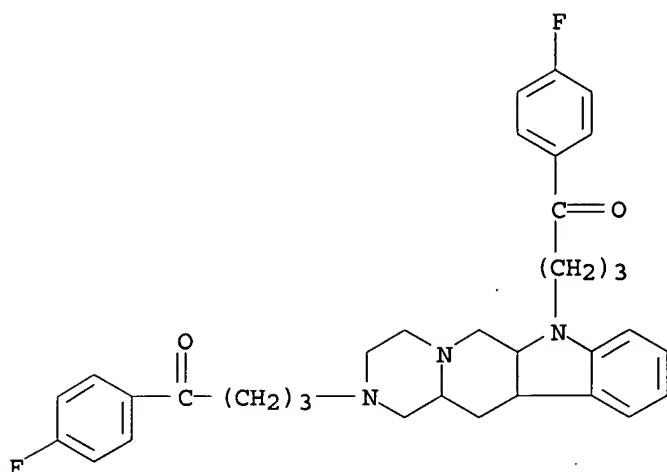
=> d scan l3

L3 21 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN

IN 1-Butanone, 4,4'-(1,3,4,6,6a,11b,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-2,7-diyl)bis[1-(4-fluorophenyl)]-, monohydrochloride (9CI)

MF C34 H37 F2 N3 O2 . Cl H

10/ 068,114



● HCl

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

153.57

153.78

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FILE COVERS 1907 - 11 Sep 2003 VOL 139 ISS 11

FILE LAST UPDATED: 10 Sep 2003 (20030910/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 40 L3

=> d l4 1- ibib abs hitstr

YOU HAVE REQUESTED DATA FROM 40 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:251375 CAPLUS

TITLE: QSAR studies in substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indoles-a potent class of neuroleptics

AUTHOR(S): Saxena, Anil K.; Ram, Siya; Saxena, Mridula; Singh, Nidhi; Prathipati, Philip; Jain, Padam C.; Singh, H. K.; Anand, Nitya

CORPORATE SOURCE: Cattar Manzil Palace Medicinal Chemistry Division, Central Drug Research Institute, Lucknow, 226001, India

SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(9), 2085-2090
CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

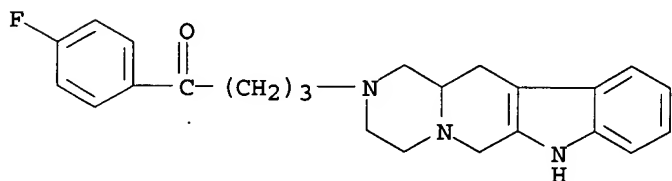
AB A series of nineteen substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indoles analogs of neuroleptic drug, Centbutindole have been studied using quant. structure-activity relationship anal. The derived models display good fits to the exptl. data ($r \geq 0.75$) having good predictive power ($rcv \geq 0.688$). The best model describes a high correlation between predicted and exptl. activity data ($r = 0.967$). Statistical anal. of the equation populations indicates that hydrophobicity (as measured by π , $\log P(o/w)$ and $SlogP_{VSA8}$), dipole μ and structural parameters in terms of indicator variable, ($In1$) and globularity are important variables in describing the variation in the neuroleptic activity in the series.

IT INDEXING IN PROGRESS

IT 42021-34-1DP, Centbutindole, analogs
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(QSAR studies in substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indoles, a potent class of neuroleptics)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:477833 CAPLUS

DOCUMENT NUMBER: 137:288014

TITLE: Basicity and coordination ability of linear hexa-amines in relation to N-(CH₂)_n-N chain-link lengths. A solution study

AUTHOR(S): Bencini, Andrea; Berni, Emanuela; Chuburu, Francoise; Giorgi, Claudia; Handel, Henri; Le Baccon, Michel; Paoletti, Piero; Valtancoli, Barbara

CORPORATE SOURCE: Department of Chemistry, University of Florence, Florence, Sesto Fiorentino, 50019, Italy

SOURCE: Polyhedron (2002), 21(14-15), 1459-1467

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis of the two new linear hexa-amines, 3,7,10,14-tetraazahexadecane-1,16-diamine (L1) and 5,9,12,16-tetraazaicosane-1,20-diamine (L2) is reported. Ligand protonation and Cu(II) and Zn(II) coordination were studied in aq. soln. by potentiometric, microcalorimetric (298.1 K, I = 0.1 mol dm⁻³) and spectrophotometric (UV-visible, ¹H and ¹³C NMR) measurements. The species present in soln. and their stability consts. were detd. L1 forms mono- and binuclear complexes in aq. soln. with Cu(II). In the [ML1]2+ complexes, the metal ion is coordinated by five N atoms, while in the [ML2]2+ complexes the metal ion is four-coordinate. This different behavior is explained in terms of the different nos. of methylene groups between adjacent N atoms.

IT 464927-98-8P 464927-99-9P

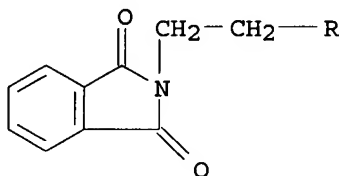
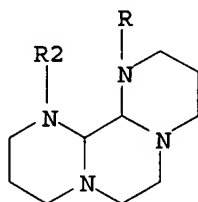
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and deprotection of)

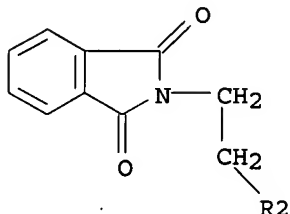
RN 464927-98-8 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2,2'-[(octahydropyrazino[1,2-a:4,3-a']dipyrimidine-1,12(2H,9H)-diyl)di-2,1-ethanediyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

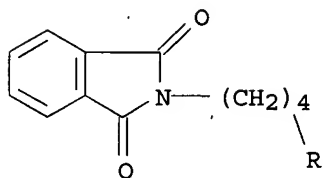
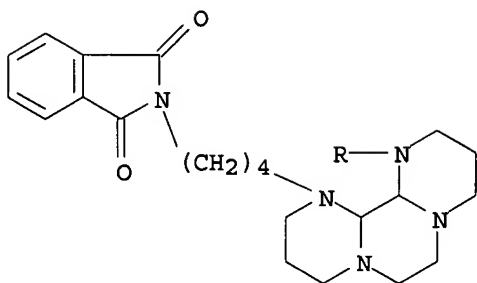


PAGE 2-A



RN 464927-99-9 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2,2'-[(octahydropyrazino[1,2-a:4,3-a']dipyrimidine-1,12(2H,9H)-diyl)di-4,1-butanediyl]bis- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:771974 CAPLUS

DOCUMENT NUMBER: 136:177415

TITLE: A sensitive LC assay for the simultaneous determination of centbutindole and its metabolite in rat serum using fluorescence detection

AUTHOR(S): Issar, Manish; Singh, Shio Kumar; Mishra, Bhrameshwar; Gupta, Ram Chandra

CORPORATE SOURCE: Pharmacokinetics and Metabolism Division, Central Drug Research Institute, Lucknow, 226001, India

SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2002), 27(1-2), 347-353

CODEN: JPBADA; ISSN: 0731-7085

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Centbutindole (:-)-2-.gamma.-[(p-fluorobenzoyl)propyl]-1,2,3,4,6,7,12,12a-octahydropyrazino(2',1':6,1)rido[3,4-b] indole (I), is a new neuroleptic agent developed by Central Drug Research Institute, India. A HPLC assay method for the simultaneous assay for I and its metabolite (II) in rat serum was developed and validated. The present method requires only 1 mL of serum with detection levels similar to that reported earlier using 4 mL serum. This assay is more suited for pre-clin. as well as phase IV studies. Linearity was obsd. between 1.25 and 40 ng/mL for I and 0.625 and 20 ng/mL for II in rat serum. Recoveries were consistent for both the analytes over the concn. ranges studied. Variation in intra- and inter-batch accuracy and precision were within acceptable limits of +/- .20% at lowest limit of quantitation, whereas at higher concns. it was +/- .15%. The assay method was employed for the study of the pharmacokinetics and metab. of I in rats. The parent compd. and its metabolites were quantitated in serum and could be monitored up to 24 h post dose.

IT 42021-34-1, Centbutindole

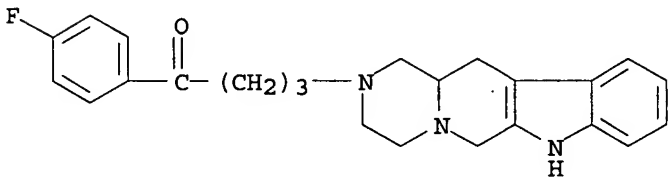
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)

(a sensitive LC assay for the simultaneous detn. of centbutindole and its metabolite in rat serum using fluorescence detection)

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RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:1004133 CAPLUS

DOCUMENT NUMBER: 124:105604

TITLE: Comparison of molecular properties of D2-receptor antagonists from different chemical families of neuroleptics

AUTHOR(S): Rusig, Isabelle; Laguerre, Michel; Carpy, Alain; Saxena, Anil K.

CORPORATE SOURCE: Laboratoire Chimie Analytique, Universite Bordeaux II, Bordeaux, 33076, Fr.

SOURCE: Medicinal Chemistry Research (1995), 5(8), 631-45
CODEN: MCREEB; ISSN: 1054-2523

PUBLISHER: Birkhaeuser

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The literature about the geometrical binding requirements of selected dopamine antagonists is discussed. Up to now, the published results were mainly concerned with semirigid compds. which mostly belonged to one single family of neuroleptics. The authors, therefore, undertook a conformational study of nine D2-receptor antagonists belonging to different chem. families, including semirigid and flexible compds., and the hitherto not studied D2-receptor antagonist (-)-centbutindole to characterize the bioactive forms. Examn. of the best structural overlap of the common features of all mols. based on a postulated active form of (S)-octoclothepepin helped in the identification of the other active conformers. At a second level of characterization, electronic and lipophilic properties of the active forms were computed to identify those properties responsible for the modulation of receptor recognition.

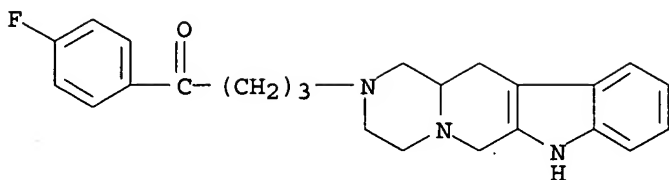
IT 42021-34-1

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

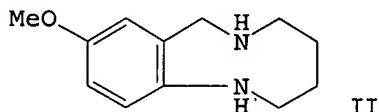
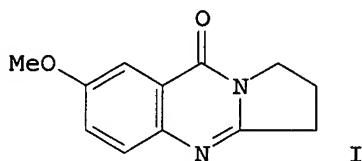
(comparison of mol. properties of D2-receptor antagonists from different chem. families of neuroleptics)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1994:269233 CAPLUS
 DOCUMENT NUMBER: 120:269233
 TITLE: Sodium borohydride-boron trifluoride etherate, a convenient and efficient reagent for the reduction of amides
 AUTHOR(S): Sengupta, Sreela; Sahu, Devi P.; Chatterjee, Sunil K.
 CORPORATE SOURCE: Div. Chem. Technol., Central Drug Res. Inst., Lucknow, 226 001, India
 SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1994), 33B(3), 285-7
 CODEN: IJSBDB; ISSN: 0376-4699
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 120:269233
 GI



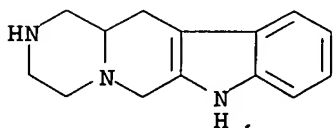
AB Sodium borohydride-boron trifluoride etherate has been employed as a reducing agent for the conversion of amides into amines, the reducing species being diborane generated in situ. This method successfully reduces primary, secondary and tertiary amides, lactams and chiral diketopiperazines, in moderate to high yields. An unusual ring cleavage is obsd. in the redn. of the pyrrolo[2,1-b]quinazolin-1-one (I) resulting in the formation of benzo-1,6-diazonine (II).

IT 55344-28-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-(9CI) (CA INDEX NAME)



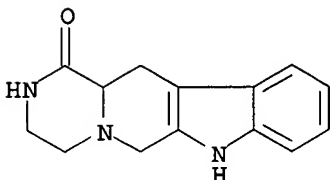
IT 55344-27-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(redn. of, to amine with sodium borohydride-boron trifluoride
ethereate)

RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro-
(9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1993:124563 CAPLUS

DOCUMENT NUMBER: 118:124563

TITLE: A process for the synthesis of 2,7-bis-.gamma.-[(4-fluorobenzoyl)propyl]-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[2',1':6,1]pyrido(3,4-b)indole useful as potential CNS depressant agent

INVENTOR(S): Rao, Jyoti; Saxena, Anil Kumar; Dua, Prithvi Raj; Shankar, Girja; Bhalla, Vishwa Nath

PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India), India

SOURCE: Indian, 6 pp.

CODEN: INXXAP

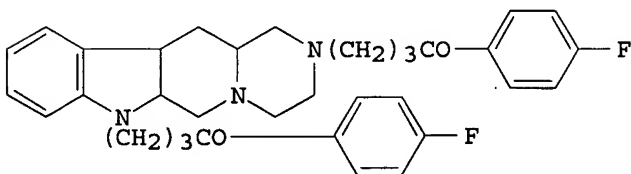
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 168877	A	19910629	IN 1987-DE1080	19871216
PRIORITY APPLN. INFO.: GI			IN 1987-DE1080	19871216



I

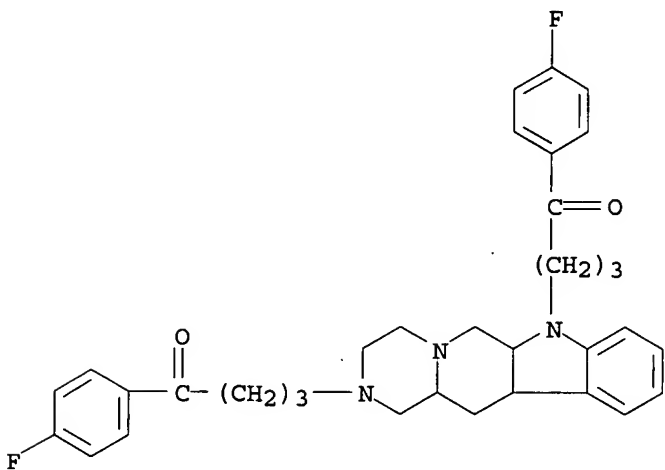
AB Title compd. (I), useful for treatment of psychic disorders (no data) was prep'd. by condensation of 1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[2',1':6,1]pyrido(3,4-b)indole (II) with 4-FC₆H₄CO(CH₂)₃Cl (III) at 30-120.degree. in presence of base and org. solvent. III in DMF was added to II, NaCO₃ and NaI in DMF, stirred at 70.degree. for 12 h to give I isolated as the HCl salt.

IT 146368-72-1P 146368-73-2P

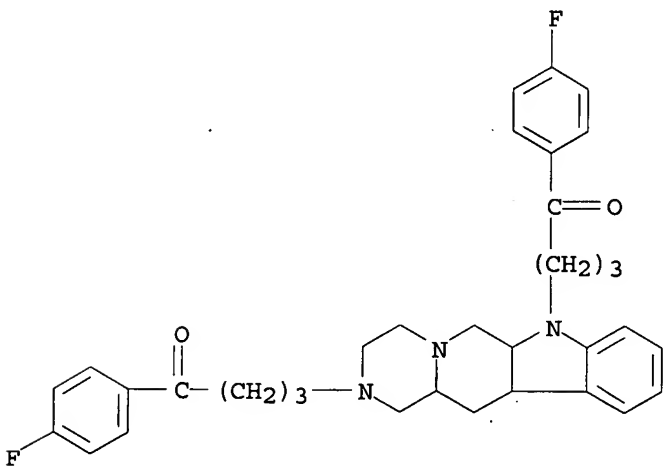
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as central nervous system depressant agent)

RN 146368-72-1 CAPLUS

CN 1-Butanone, 4,4'-(1,3,4,6,6a,11b,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-2,7-diyl)bis[1-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 146368-73-2 CAPLUS
 CN 1-Butanone, 4,4'-(1,3,4,6,6a,11b,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-2,7-diyl)bis[1-(4-fluorophenyl)-, monohydrochloride (9CI)
 (CA INDEX NAME)



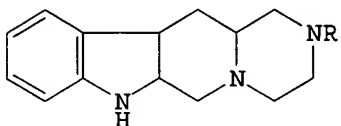
● HCl

L4 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1992:591872 CAPLUS
 DOCUMENT NUMBER: 117:191872
 TITLE: Process for synthesis of novel 2-substituted-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[2,1:6,1]pyrido[3,4-b]indoles
 INVENTOR(S): Rao, Jyoti; Saxena, Anil Kumar; Saxena, Ram Mohan; Dua, Prithviraj; Srimal, Rikhab Chand; Bhalla, Vishnunath
 PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India), India
 SOURCE: Indian, 6 pp.

10/ 068,114

CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 166420	A	19900505	IN 1988-DE73	19880129
PRIORITY APPLN. INFO.:			IN 1988-DE73	19880129
OTHER SOURCE(S):	MARPAT 117:191872			
GI				



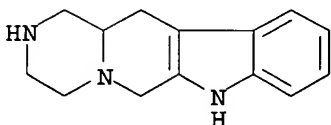
AB Title compds. I (R = H, alkyl) useful as starting materials for central nervous system and cardiovascular (sic) active agents, are prepd. by redn. of the octahydro deriv. at -20 to +5.degree. in 15 min to 24 h. Borane Me sulfide in soln. was added to the octahydro deriv. of I (R = H) in F3CCO2H at 0 to 50.degree. under N, then the reaction mixt. was stirred for 2 h at 34.degree. to give after basification I (R = H).

IT 55344-28-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(redn. of, by borane Me sulfide)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:542817 CAPLUS

DOCUMENT NUMBER: 117:142817

TITLE: Single oral dose pharmacokinetics of centbutindole, a new neuroleptic agent, in healthy human volunteers
AUTHOR(S): Paliwal, J. K.; Gupta, R. C.; Grover, P. K.; Asthana, O. P.; Nityanand, S.

CORPORATE SOURCE: Pharmacokinet. Metab. Div., Cent. Drug Res. Inst., Lucknow, India

SOURCE: Drug Investigation (1992), 4(3), 246-51
CODEN: DRUIEA; ISSN: 0114-2402

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pharmacokinetics of centbutindole compd. were investigated after oral administration of single 3 mg tables in 5 healthy male volunteers. Serum levels of the unchanged drug were measured by high pressure liq. chromatog. (HPLC) with fluorescence detection. Mean peak serum levels (3.48 +/- 1.58 mg/L) were reached at 4 h, and the mean biol. half-life was calcd. as 12.45 +/- 3.59 h. The data were best fitted to a

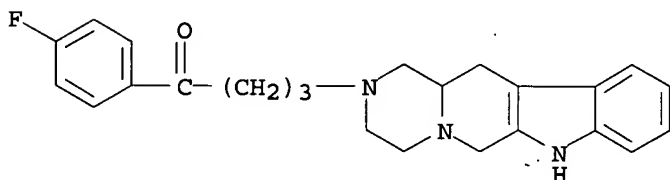
1-compartment open model with first-order absorption and elimination kinetics. Considerable intersubject variability was noted in the absorption characteristics of centbutindole, and further study is planned to better define the pharmacokinetics of this drug.

IT 42021-34-1

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetics of, in humans)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:462715 CAPLUS

DOCUMENT NUMBER: 117:62715

TITLE: Antihistaminic activity of quinethindole: a 2-substituted pyrazinopyridoindole derivative

AUTHOR(S): Patnaik, G. K.; Saxena, A. K.; Saxena, M.; Srimal, R. C.

CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India

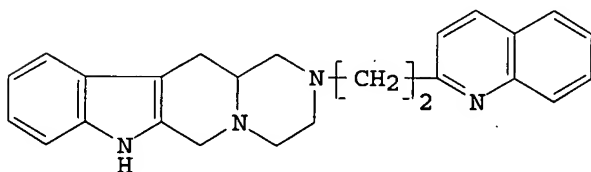
SOURCE: Indian Journal of Experimental Biology (1992), 30(2), 144-6

CODEN: IJEBA6; ISSN: 0019-5189

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

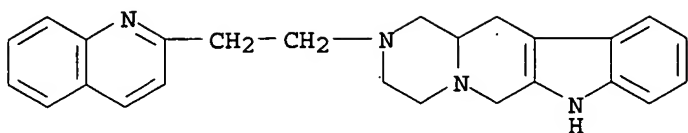
AB Quinethindole (I), a 2-substituted pyrazinopyridoindole, showed specific antihistaminic H1 activity in various in vivo and in vitro test models. It also inhibited antigen-induced contraction of ileum of sensitized guinea pig. The antihistaminic activity was of competitive nature.

IT 42021-23-8, Quinethindole

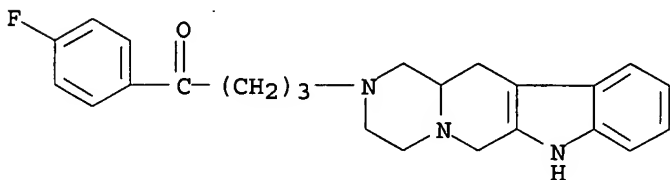
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antihistaminic H1 activity of)

RN 42021-23-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(2-quinolinyl)ethyl]- (9CI) (CA INDEX NAME)



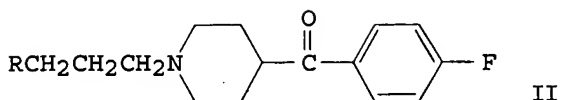
L4 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1992:50746 CAPLUS
 DOCUMENT NUMBER: 116:50746
 TITLE: Simultaneous determination of centbutindole and its hydroxy metabolite in serum by high-performance liquid chromatography
 AUTHOR(S): Paliwal, Jyoti Kumar; Gupta, Ram Chandra; Grover, Pyara Krishen; Asthana, Omkar P.; Nityanand, Swaran
 CORPORATE SOURCE: Pharmacokinet. Metab. Div., Cent. Drug. Res. Inst., Lucknow, 226001, India
 SOURCE: Journal of Chromatography (1991), 572(1-2), 219-25
 CODEN: JOCRAM; ISSN: 0021-9673
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A high-performance liq. chromatog. assay has been developed and validated for the detn. of centbutindole and its hydroxy metabolite in serum. The method involves extn. of serum samples with di-Et ether at pH > 8, back-extn. into 0.5 M hydrochloric acid and finally again with di-Et ether after addn. of 2 M potassium hydroxide. Sepn. was accomplished by reversed-phase high-performance liq. chromatog. on a cyano column with an acetonitrile-phosphate buffer system. The recovery of centbutindole and its metabolite was always greater than 80%. Calibration curves were linear over the concn. range 0.25-5 ng/mL for centbutindole and 0.05-1 ng/mL for the hydroxy metabolite. Although the lower limit of detection was 0.1 ng/mL for centbuntindole and 0.02 ng/mL for the hydroxy metabolite, the reliable limits of quantitation were 0.25 and 0.05 ng/mL, resp., using 4 mL of serum.
 IT 42021-34-1, Centbutindole
 RL: ANT (Analyte); ANST (Analytical study)
 (detn. of, in blood of humans by HPLC)
 RN 42021-34-1 CAPLUS
 CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1991:6251 CAPLUS
 DOCUMENT NUMBER: 114:6251
 TITLE: Synthesis and SAR studies in 1-(.gamma.-substituted propyl)-4-(4-fluorobenzoyl/fluorobenzyl)piperidines as potential CNS agents
 AUTHOR(S): Tripathi, Ravish C.; Singh, H. K.; Saxena, Anil K.
 CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India

10/ 068,114

SOURCE: Indian Journal of Chemistry, Section B: Organic
Chemistry Including Medicinal Chemistry (1990),
29B(9), 865-9
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:6251
GI



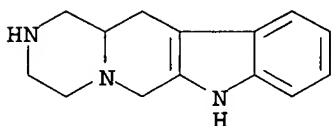
AB The key intermediate 1-(.gamma.-chloropropyl)-4-(4-fluorobenzoyl)piperidine has been prepd. by the condensation of 4-(4-fluorobenzoyl)piperidine (I) with 1-bromo-3-chloropropane. This on reaction with different amines, thiophenols and piperazines gives the title compds. II (R = sec-amine, thiolate). Compd. I on reaction with trans-2-phenoxyethylcyclopropane-1-carbonyl chloride yields trans-1-[4-(4-fluorobenzoyl)piperidin-1-ylcarbonyl]-2-phenoxyethylcyclopropane. Some of these compds. show potent CNS activity.

IT 55344-28-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with (chloropropyl)(fluorobenzoyl)piperidine)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-(9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:611944 CAPLUS

DOCUMENT NUMBER: 113:211944

TITLE: Synthesis, biological evaluation, and quantitative structure-activity relationship analysis of [.beta.-(aroylamino)ethyl]piperazines and -piperidines and [2-[(arylamino)carbonyl]ethyl]piperazines, -piperidines, -pyrazinopyridoindoles, and -pyrazinoisoquinolines. A new class of potent H1 antagonists

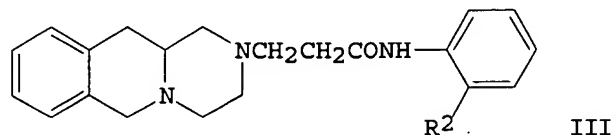
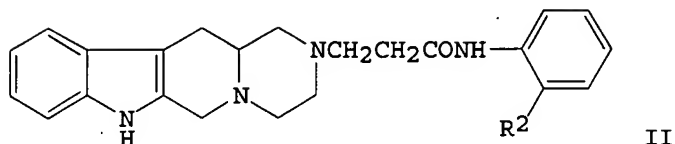
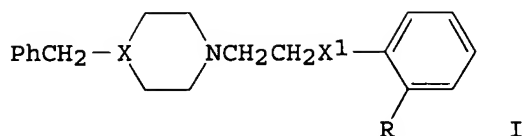
AUTHOR(S): Saxena, Mridula; Agarwal, Shiv K.; Patnaik, G. K.; Saxena, Anil K.

CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Journal of Medicinal Chemistry (1990), 33(11), 2970-6
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 113:211944
GI



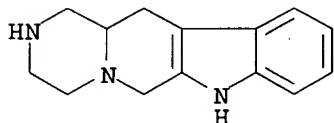
AB The title compds. I (R = H, Me, Et, Br, Cl, F, iodo, NO₂; X = CH, N; X₁ = CONH, NHCO), II and III (R₂ = H, MeO, Et, Cl, F, NO₂) were prepd. and their H₁-antagonistic activity studied in isolated guinea pig ileum. Quant. structure-activity relationship anal. indicates that the hydrophobicity of the side chain of these compds. plays a major role in their activity while steric and electronic factors are of secondary importance. All acted on a common receptor and appear to interact similarly with the receptor.

IT 55344-28-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with bromopropionamides)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-(9CI) (CA INDEX NAME)



L4 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:611942 CAPLUS

DOCUMENT NUMBER: 113:211942

TITLE: Synthesis and biological activities of
trans-1-substituted-2(phenoxymethyl)cyclopropanes
AUTHOR(S): Tripathi, Ravish C.; Saxena, Anil K.; Anand, Nitya
CORPORATE SOURCE: Cent. Drug. Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic
Chemistry Including Medicinal Chemistry (1990),
29B(5), 455-8

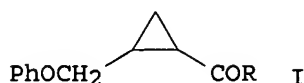
CODEN: IJSBDB; ISSN: 0376-4699

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 113:211942

GI



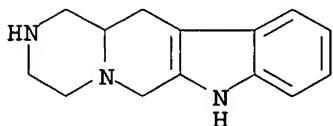
AB trans-2-Phenoxymethylcyclopropanecarboxylic acid chloride I (R = Cl) was reacted with amines to give the substitution products I (e.g., R = NHNH₂, NHNHPh, NHC₆H₄OH-2, NHC₆H₃Cl₂-2,6). Conversion of I (R = Cl) to the corresponding amine was also achieved in 3 steps. The prepd. compds. were tested for biol. activity. Some showed significant diuretic, antiinflammatory, and hypotensive activity.

IT 55344-28-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with (phenoxymethyl)cyclopropanecarboxylic acid)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-(9CI) (CA INDEX NAME)



L4 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:597746 CAPLUS

DOCUMENT NUMBER: 113:197746

TITLE: Analytical and shelf-life studies on centbutindole, a new neuroleptic compound

AUTHOR(S): Seth, R. K.; Sarin, J. P. S.

CORPORATE SOURCE: Div. Pharm., Cent. Drug Res. Inst., Lucknow, 226 001, India

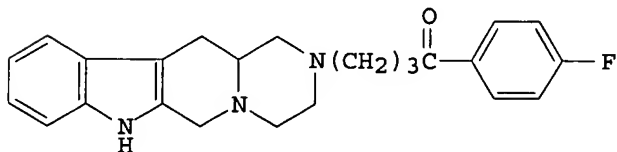
SOURCE: Indian Journal of Pharmaceutical Sciences (1989), 51(6), 244-7

CODEN: IJSIDW; ISSN: 0250-474X

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Centbutindole (I) was stable in pharmaceuticals (capsules, tablets, and injections) for 4 yr at room temp. No change in general appearance, TLC pattern, UV absorption pattern, and drug content was obsd. on heating I at 100.degree. for 6 h. A UV spectrophotometric method was convenient for the detn. of I in dosage forms.

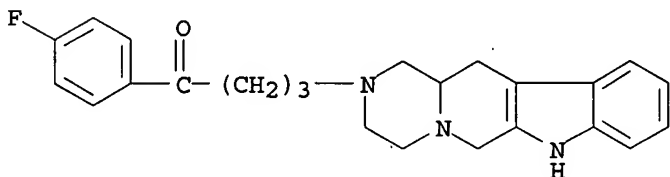
IT 42021-34-1, Centbutindole

RL: BIOL (Biological study)

(stability in pharmaceuticals of, UV spectrophotometric and TLC study of)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:545612 CAPLUS

DOCUMENT NUMBER: 113:145612

TITLE: Effect of melanotropin release inhibiting factor on changes by haloperidol and centbutindole in cerebral cortical 5-hydroxytryptamine receptors

AUTHOR(S): Gulati, Anil; Bhargava, Hemendra N.

CORPORATE SOURCE: Chicago Health Sci. Cent., Univ. Illinois, Chicago, IL, 60612, USA

SOURCE: Pharmacology (1990), 41(2), 98-106

CODEN: PHMGBN; ISSN: 0031-7012

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of melanotropin release inhibiting factor (Pro-Leu-Gly-NH₂, MIF) was detd. on changes induced by 2 neuroleptics, haloperidol and centbutindole, in cerebral cortical 5-HT receptors. Male Sprague-Dawley rats were injected daily i.p. with vehicle, haloperidol (1.0 mg/kg), or centbutindole (0.5 mg/kg), resp., for 21 days. On day 22, these 3 groups were further divided into 2 subgroups and injected with either vehicle or MIF (2.0 mg/kg, i.p.) daily for 3 days. [3H]-5-HT was used to study 5-HT₁ receptors, and [3H]spiroperidol to label 5-HT₂ receptors in the cerebral cortex. Chronic administration of haloperidol increased (39.7%) the maximal binding capacity (B_{max}) of [3H]-5-HT binding to 5-HT₁ receptors. Dissocn. const. (K_d) values did not change. Centbutindole had no effect on 5-HT₁ receptors. MIF had no effect on 5-HT₁ receptors, nor did it alter haloperidol-induced increases in the B_{max} of [3H]-5-HT binding to 5-HT₁ receptors. Chronic administration of centbutindole increased (61.1%) the B_{max} of [3H]spiroperidol binding to 5-HT₂ receptors. No change occurred in the K_d values. Chronic treatment with haloperidol had no effect on 5-HT₂ receptor characteristics. MIF had no effect on 5-HT₂ receptors or on the increase in 5-HT₂ receptor d. induced by centbutindole. The behavioral syndrome induced by 5-HTP (50, 100, and 200 mg/kg, i.p.) was also measured in rats treated chronically with haloperidol or centbutindole. Haloperidol had no effect on the 5-HTP syndrome, whereas centbutindole stimulated by 24-45% the intensity of the syndrome. MIF had no effect on the 5-HTP syndrome, nor did it alter the increase induced by centbutindole. Evidently, haloperidol and centbutindole differentially affect cortical 5-HT₁ and 5-HT₂ receptors. MIF does not by itself affect 5-HT receptors, nor does it reverse the up-regulation of 5-HT receptors induced by haloperidol and centbutindole.

IT 42021-34-1, Centbutindole

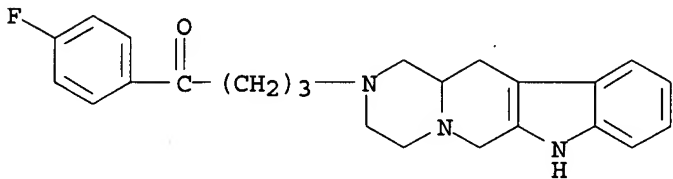
RL: BIOL (Biological study)

(serotonin receptor subtypes differential response to, in cerebral cortex, melanotropin release inhibiting factor action in relation to)

10/ 068,114

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:235217 CAPLUS

DOCUMENT NUMBER: 112:235217

TITLE: Synthesis and structure-activity relationship in [(aryloxy)alkyl]amines

AUTHOR(S): Agarwal, Shiv K.; Saxena, Anil K.; Jain, Padam C.; Anand, Nitya; Sur, R. N.; Srimal, R. C.; Dhawan, Bhola N.

CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, 226 001, India

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1990), 29B(1), 80-4

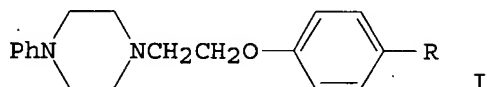
CODEN: IJSBDB; ISSN: 0376-4699

DOCUMENT TYPE: Journal

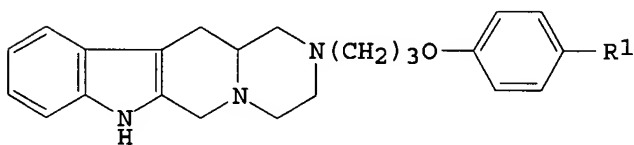
LANGUAGE: English

OTHER SOURCE(S): CASREACT 112:235217

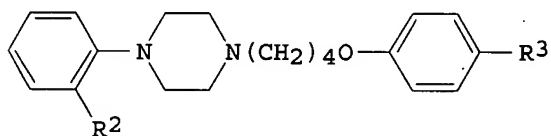
GI



I



II



III

AB [(Aryloxy)alkyl]piperazine derivs. I (R = NO₂, CHO, Br), II (R₁ = NO₂, F, NH₂), and III (R₂ = H, R₃ = NO₂, CHO, CH₂OH; R₂ = OMe, R₃ = NO₂, NH₂) were prepd. and tested for central nervous system-depressant, antihistaminic, hypotensive, antiinflammatory, antiarrhythmic, diuretic, and anaphylaxis-inhibitory activity. All showed gross behavior-depressant activity and II (R = F) showed antihistaminic activity.

IT 55344-28-0

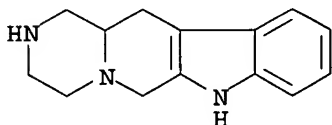
RL: RCT (Reactant); RACT (Reactant or reagent)

10/ 068,114

(substitution reaction of, with (aryloxy)chloropropanes)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)



L4 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1989:97553 CAPLUS

DOCUMENT NUMBER: 110:97553

TITLE: Organic solvent-soluble, oxide-supported hydrogenation catalyst precursors

INVENTOR(S): Edlund, David J.; Finke, Richard G.; Saxton, Robert J.

PATENT ASSIGNEE(S): University of Oregon, USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8806489	A1	19880907	WO 1988-US609	19880226
W: AU, JP, NO, SU, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8814208	A1	19880926	AU 1988-14208	19880226
US 5116796	A	19920526	US 1988-275105	19881026
PRIORITY APPLN. INFO.:			US 1987-20122	19870227
			WO 1988-US609	19880226

OTHER SOURCE(S): MARPAT 110:97553

AB Catalyst precursors Ax(LnIr(I).X2M15M13O62]x- (A = counteranion; L = olefinic ligand or dioxygen; M = W, Mo; M1 = Nb, V, Ti, Zr, Ta, Hf; X = B, Si, Ge, P, As, Se, Te, I, Co, Mn, Cu; n = 1, 2; x = .ltoreq.15), useful as precursors for the manuf. of org. solvent-sol. hydrogenation catalysts, are prepd. (Bu4N)8[(COD)Ir.P2W15Nb3O62].Bu4NBF4.9H2O (COD = 1,5-cyclooctadiene) was prepd. by adding a degassed soln. of (Bu4N)9P2W15Nb3O62 to a degassed acetonitrile soln. of [Ir(COD)(CH3CN)2]BF4.

IT 114672-71-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, in hydrogenation catalyst precursor manuf.)

RN 114672-71-8 CAPLUS

CN Niobate(9-), [heptacos-.mu.-oxopentadeca-oxo[.mu.9-[phosphato(3-)-O:O:O:O':O':O':O':O':O':O']pentadecatungstate]nona-.mu.-oxotrioxo[.mu.9-[phosphato(3-)-O:O:O:O':O':O':O':O':O':O']tri-, nonahydrogen, compd. with 2,3,4,6,7,8,9,10-octahydropyrazino[1,2-a]azepine (1:9), undecahydrate (9CI) (CA INDEX NAME)

CM 1

CRN 114672-70-7

CMF H . 1/9 Nb3 O62 P2 W15

CCI CCS

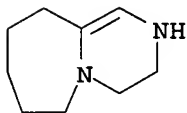
10/ 068,114

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 114672-69-4

CMF C9 H16 N2



L4 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1988:493246 CAPLUS

DOCUMENT NUMBER: 109:93246

TITLE: Trisubstituted heteropolytungstates as soluble metal oxide analogues. 4. The synthesis and characterization of organic solvent-soluble (Bu₄N)₁₂H₄P₄W₃ONb₆O₁₂₃ and (Bu₄N)₉P₂W₁₅Nb₃O₆₂ and solution spectroscopic and other evidence for the supported organometallic derivatives (Bu₄N)₇[(C₅Me₅)Rh.cntdot.P₂W₁₅Nb₃O₆₂] and (Bu₄N)₇[(C₆H₆)Ru.cntdot.P₂W₁₅Nb₃O₆₂]

AUTHOR(S): Edlund, David J.; Saxton, Robert J.; Lyon, David K.; Finke, Richard G.

CORPORATE SOURCE: Dep. Chem., Univ. Oregon, Eugene, OR, 97403, USA

SOURCE: Organometallics (1988), 7(8), 1692-704

CODEN: ORGND7; ISSN: 0276-7333

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 109:93246

AB The synthesis and characterization of the previously unknown triniobium-substituted Dawson heteropolyanion, P₂W₁₅Nb₃O₆₂₉-, as its org. solvent sol. Bu₄N⁺ salt, are described. The monomer P₂W₁₅Nb₃O₆₂₉- undergoes formation of a previously unknown Nb-O-Nb bridged species: 2P₂W₁₅Nb₃O₆₂₉- + 2H⁺.dblharw. H₂O + P₄W₃₀Nb₆O₁₂₃₁₆-. The initial synthesis, at pH 4.6, yields the Me₄N⁺ salt of this aggregate, (Me₄N)₁₂H₄P₄W₃₀Nb₆O₁₂₃. Metathesis with Bu₄N⁺ provides the Bu₄N⁺ salt, (Bu₄N)₁₂H₄P₄W₃₀Nb₆O₁₂₃. Cleavage/deprotonation of the latter salt with 6 equiv of Bu₄NOH yields (Bu₄N)₉P₂W₁₅Nb₃O₆₂, which has been shown to form covalently attached, polyoxoanion-supported (C₅Me₅)Rh₂⁺ and (C₆H₆)Ru₂⁺ complexes of C_{3v} symmetry in acetonitrile soln. by IR, ¹H NMR, ³¹P NMR, and ¹⁸³W NMR spectroscopy, soln. mol. wt. measurements, and tests with ion-exchange resins.

IT 114672-71-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 114672-71-8 CAPLUS

CN Niobate(9-), [heptacosia-.mu.-oxopentadeca-oxo[.mu.9-[phosphato(3-)-O:O:O:O':O':O':O':O']:]pentadecatungstate]nona-.mu.-oxotrioxo[.mu.9-[phosphato(3-)-O:O:O:O':O':O':O':O']:]tri-, nonahydrogen, compd. with 2,3,4,6,7,8,9,10-octahydropyrazino[1,2-a]azepine (1:9), undecahydrate (9CI) (CA INDEX NAME)

CM 1

CRN 114672-70-7

CMF H . 1/9 Nb3 O62 P2 W15

CCI CCS

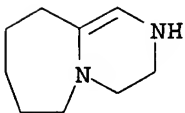
10/ 068,114

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

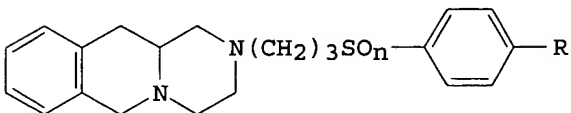
CM 2

CRN 114672-69-4

CMF C9 H16 N2



L4 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:422938 CAPLUS
DOCUMENT NUMBER: 109:22938
TITLE: Synthesis of N-[3-aryl(thio/sulfono)propyl]heterocycli
cs as potential CNS/CVS agents
AUTHOR(S): Rao, Jyoti; Saxena, Anil K.; Saxena, R. M.; Singh, H.
K.; Kar, K.; Srimal, R. C.
CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, 226
001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic
Chemistry Including Medicinal Chemistry (1987),
26B(8), 761-5
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:22938
GI



I

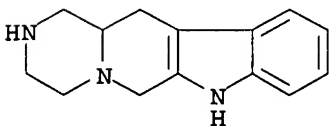
AB Condensation of 4-RC6H4SO_n(CH₂)₃Cl (n = 0, R = NHAc, OMe, Me; n = 2, R' = NHAc) with 1-benzylpiperazine, 4-benzylpiperidine, octahydropyrazinoisoquinoline, and octahydropyrazinopyridoindole gave the corresponding adducts, e.g., I, in 44-83% yields. Hydrolysis of the acetamido derivs. gave the corresponding amino derivs., e.g. I (n = 0, R = NH₂, II). Reductive methylation of II gave I (R = NMe₂). These compds. exhibit good hypotensive, antiinflammatory, diuretic, anxiolytic and passive cutaneous anaphylaxis activities.

IT 55344-28-0

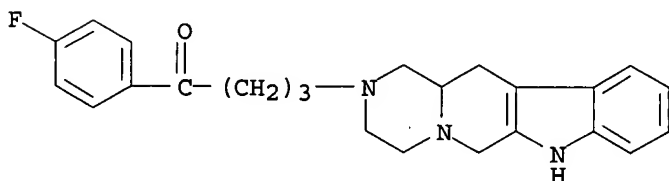
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, with arylthio- and arylsulfonyl chlorides)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)



L4 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1988:400681 CAPLUS
 DOCUMENT NUMBER: 109:681
 TITLE: Differential alteration in striatal dopaminergic and cortical serotonergic receptors induced by repeated administration of haloperidol or centbutindole in rats
 AUTHOR(S): Gulati, Amir; Srimal, R. C.; Dhawan, B. N.
 CORPORATE SOURCE: Coll. Pharm., Univ. Illinois, Chicago, IL, 60612, USA
 SOURCE: Pharmacology (1988), 36(6), 396-404
 CODEN: PHMGBN; ISSN: 0031-7012
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Centbutindole is a new neuroleptic drug having a pharmacol. profile similar to haloperidol, but it does not cause hypothermia and has a higher sepn. between doses causing catalepsy and neurolepsy. The interactions of centbutindole with striatal dopamine and cortical 5-HT₂ receptors have been studied along with haloperidol. Rats received haloperidol (1.0 mg/kg, p.o.), centbutindole (0.5 mg/kg, p.o.) or saline daily for 21 days. Following drug withdrawal for 3 days, apomorphine (0.1-1.0 mg/kg, i.p.) or 5-hydroxytryptamine (5-HTP, 50-200 mg/kg, i.p.) was injected. Apomorphine-induced stereotyped behavior was potentiated in the haloperidol-treated rats, while the 5-HTP-induced behavioral syndrome was increased in centbutindole-treated rats. Receptor binding studies indicated an increase in the maximal binding capacity B_{max} of striatal dopamine receptor (29.4%) in haloperidol-treated and of cortical 5-HT₂ receptor (17.8%) in centbutindole-treated animals. No change in the apparent dissocn. const. K_d was obsd. Repeated treatment with haloperidol produced striatal dopamine receptor supersensitivity, while centbutindole treatment produced cortical serotonergic receptor supersensitivity.
 IT 42021-34-1
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (dopaminergic and serotonergic receptors of brain response to)
 RN 42021-34-1 CAPLUS
 CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

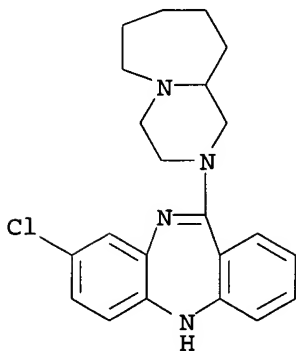


L4 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1987:617657 CAPLUS
 DOCUMENT NUMBER: 107:217657
 TITLE: 11-[N-(Diazabicyclo[4.m.0]alkanyl)]-5H-dibenzo[b,e][1,4]diazepines with neuroleptic activity
 INVENTOR(S): Likhoshervostov, A. M.; Raevskii, K. S.; Stavrovskaya, A. V.; Skoldinov, A. P.; Rostock, Angelika; Rueger, Carla; Roehnert, Helmut
 PATENT ASSIGNEE(S): Scientific-Research Institute of Pharmacology, Academy of Medical Sciences, U.S.S.R., USSR; VEB Arzneimittelwerk Dresden
 SOURCE: U.S.S.R. From: Otkrytiya, Izobret. 1986, (46), 296.

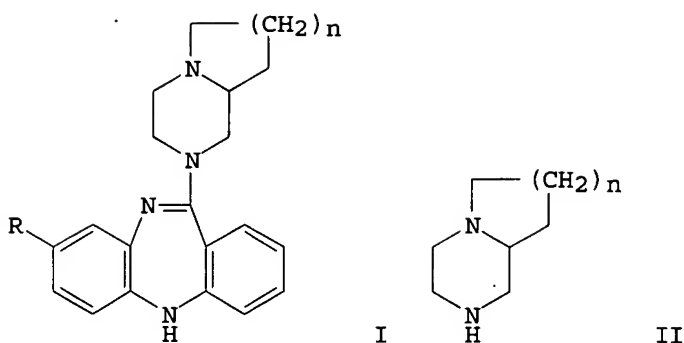
10/ 068,114

DOCUMENT TYPE: CODEN: URXXAF
LANGUAGE: Patent
FAMILY ACC. NUM. COUNT: 1 Russian
PATENT INFORMATION:

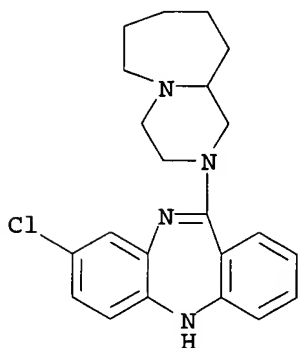
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SU 1015618	A1	19861215	SU 1980-2923128	19800128
PRIORITY APPLN. INFO.:			SU 1980-2923128	19800128
GI	For diagram(s), see printed CA Issue.			
AB	The title compds. (I; R = H, m = 3; R = Cl, m = 3-5) have neuroleptic activity (no data).			
IT	81469-87-6			
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (neuroleptic activity of)			
RN	81469-87-6 CAPLUS			
CN	5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl) - (9CI) (CA INDEX NAME)			



L4 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:220842 CAPLUS
DOCUMENT NUMBER: 102:220842
TITLE: Synthesis and neuroleptic effects of new
11-substituted 5H-dibenzo[b,e][1,4]diazepines
AUTHOR(S): Skoldinov, A. P.; Raevskii, K. S.; Likhoshesterov, A.
M.; Stavrovskaya, A. V.; Rueger, Carla; Rostock,
Angelika; Roehnert, H.
CORPORATE SOURCE: Inst. Pharmacol. Med. Sci., Moscow, 125315, USSR
SOURCE: Pharmazie (1984), 39(12), 812-13
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 102:220842
GI

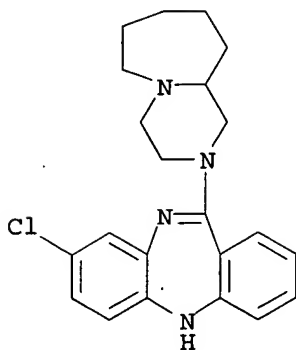


- AB The title compds. (I; R = H, n = 1; R = Cl, n = 1-3), prepd. in 42.0-64.4% yield by treating a dibenzodiazepinone with a perhydro fused-ring pyrazine (II) in the presence of TiCl_4 , were tested for neuroleptic activity. I (R = Cl, n = 1) was the most effective in these tests.
- IT **81469-87-6P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (prepn. and neuroleptic activity of)
- RN 81469-87-6 CAPLUS
- CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl) - (9CI) (CA INDEX NAME)



- IT **81469-88-7P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)
- RN 81469-88-7 CAPLUS
- CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl) -, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
- CM 1
- CRN 81469-87-6
- CMF C22 H25 Cl N4

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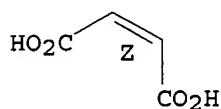


CM 2

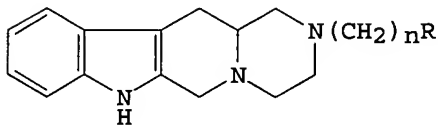
CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



L4 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:455059 CAPLUS
DOCUMENT NUMBER: 101:55059
TITLE: Synthesis and QSAR in 2-substituted
1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[
3,4-b]indoles - a new class of H1-antagonists
AUTHOR(S): Saxena, Anil K.; Dhaon, Madhup K.; Ram, Siya; Saxena,
Mridula; Jain, Padam; Patnaik, G. K.; Anand, Nitya
CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic
Chemistry Including Medicinal Chemistry (1983),
22B(12), 1224-32
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Pyrazinopyridoindoles I [R = (un)substituted PhCONH, Ph2CHO, etc.; n = 2, 3] were prepd. and tested for their H1-receptor antagonistic action in guinea pig ileum. The quant. structure-activity anal. of 34 compds. showed that the activity is influenced by hydrophobicity of the side chain and by the bulk of the substituent at the ortho-position of the Ph ring of the .beta.-aroylaminoethyl side chain. Comparing these results with those of diphenylhydramine suggests that the Ph ring of the side chain and N2 of

10/ 068,114

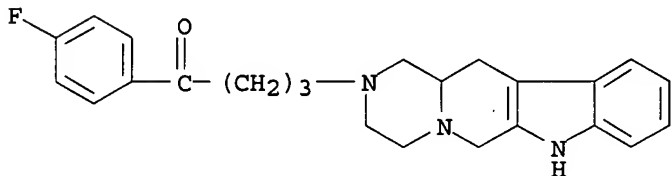
I (R = PhCONH, n = 2) could occupy the same receptor sites as 1 of the Ph rings of diphenylhydramine and its tertiary N.

IT 42021-34-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(Grignard reaction of, with Me iodide)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

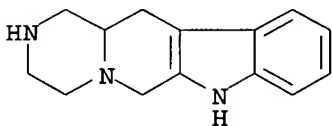


IT 55344-28-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyanoalkylation of)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1984:174024 CAPLUS

DOCUMENT NUMBER: 100:174024

TITLE: The chemistry of an isolable azomethine ylide

AUTHOR(S): Huisgen, Rolf; Niklas, Karl

CORPORATE SOURCE: Inst. Org. Chem., Univ. Muenchen, Munich, D-8000/2, Fed. Rep. Ger.

SOURCE: Heterocycles (1984), 22(1), 21-6

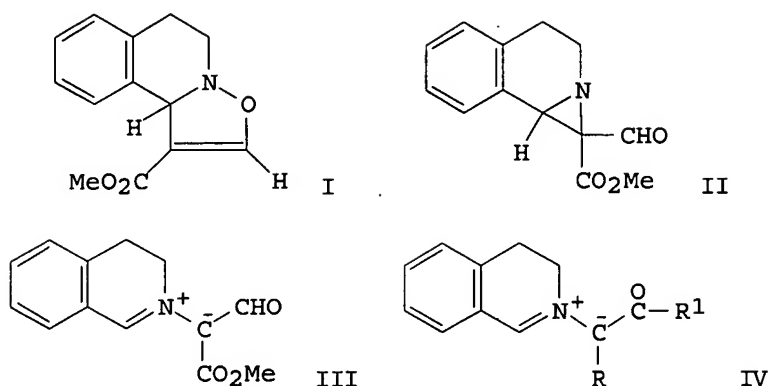
CODEN: HTCYAM; ISSN: 0385-5414

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 100:174024

GI



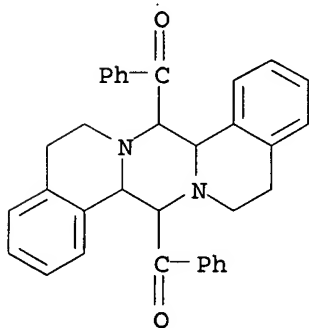
AB The 4-isoxazoline I undergoes ring contraction to the acylaziridine II which is converted to the azomethine ylide III. The small influence of solvent polarity on the rate const. of the conversion I \rightarrow III suggests a mechanism via a trimethylene type species for the rate-detg. step. Whereas III is the first azomethine ylide which can be isolated without being stabilized by arom. resonance, the ylides IV (R = H, CO₂N; R₁ = Me, Ph) dimerize to piperazine derivs. 1,3-Dipolar cycloaddns. of the azomethine ylides III and IV are described.

IT 89768-86-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 89768-86-5 CAPLUS

CN Methanone, (5,6,8,8a,13,14,16,16a-octahydropyrazino[2,1-a:5,4-a']diisoquinoline-8,16-diyl)bis[phenyl- (9CI) (CA INDEX NAME)



L4 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1984:34500 CAPLUS

DOCUMENT NUMBER: 100:34500

TITLE: Studies in potential filaricides: Part XIII-Synthesis of 1,4-diazabicyclo[4.3.0]nonanes, 1,4-diazabicyclo[4.4.0]decanes and 1,4-diazabicyclo[4.5.0]undecanes as diethylcarbamazine analogs

AUTHOR(S): Shukla, U. K.; Khanna, J. M.; Sharma, Satyavan; Anand, Nitya; Chatterjee, R. K.; Sen, A. B.

CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, 226 001, India

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1983),

DOCUMENT TYPE:

Journal

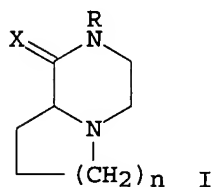
LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 100:34500

GI



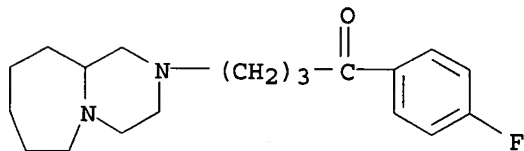
AB The title compds. I [$n = 1-3$; $X = H_2, O$; $R =$ (un)substituted alkyl, CONEt₂] were prep'd. and evaluated for their filaricidal activity against Litomosoides carinii infection in cotton rats. Except I ($n = 1$, $R =$ CONEt₂, $X = H_2$) which is .apprx.60% as active as the std. diethylcarbamazine (II), none of the other compds. shows any activity against adult worms. The results have been rationalized in terms of crit. bulk around N-1 of the piperazine ring of II. It appears that both axial and equatorial N-Me bonds in II are acceptable for activity.

IT 60390-52-5P 88327-82-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and filaricidal activity of)

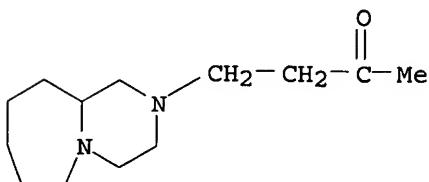
RN 60390-52-5 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(octahydropyrazino[1,2-a]azepin-2(1H)-yl) - (9CI) (CA INDEX NAME)



RN 88327-82-6 CAPLUS

CN 2-Butanone, 4-(octahydropyrazino[1,2-a]azepin-2(1H)-yl) - (9CI) (CA INDEX NAME)



L4 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

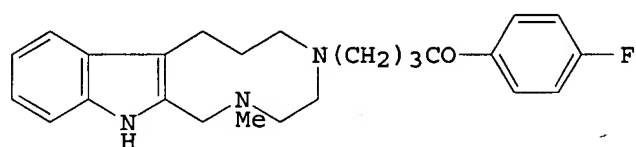
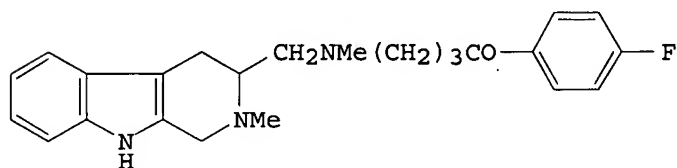
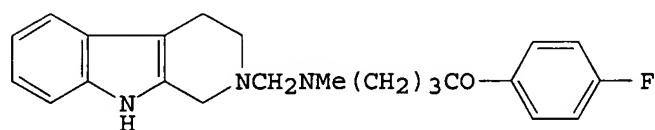
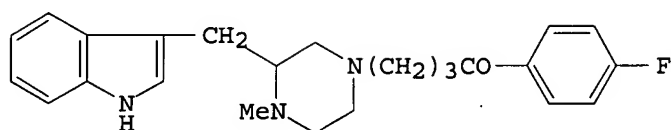
ACCESSION NUMBER: 1983:16659 CAPLUS

DOCUMENT NUMBER: 98:16659

TITLE: Agents acting on CNS. Part XXIX. Synthesis of seco analogs of centbutindole, a potent neuroleptic.

AUTHOR(S): Kumar, Naresh; Dhaon, Madhup K.; Agarwal, Shiv K.;

Saxena, Anil K.; Jain, Padam C.; Prasad, C. R.; Anand, Nitya
 CORPORATE SOURCE: Div. Med. Chem. Pharmacol. Div., Cent. Drug Res.
 Inst., Lucknow, 226001, India
 SOURCE: European Journal of Medicinal Chemistry (1982), 17(4),
 312-16
 CODEN: EJMCA5; ISSN: 0009-4374
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 98:16659
 GI



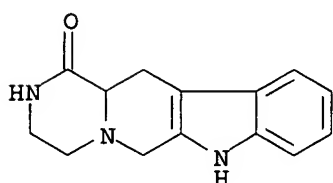
AB Four seco analogs of centbutindole I, II, III, and IV were prepd. and their tranquilizing activities detd. The reduced activities of I-IV confirm that the rigid conformations of tryptamine and piperazine moieties are essential for this activity.

IT 55344-27-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. and quaternization of, by Me iodide)

RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro-(9CI) (CA INDEX NAME)



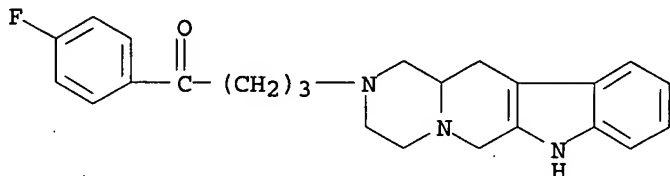
IT 42021-34-1DP, seco analogs

10/ 068,114

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl) - (9CI) (CA INDEX NAME)



L4 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1982:162757 CAPLUS

DOCUMENT NUMBER: 96:162757

TITLE: 5H-Dibenzo[b,e][1,4]diazepines substituted in the 11-position

INVENTOR(S): Rueger, Carla; Rostock, Angelika; Roehnert, Helmut; Skoldinov, A. P.; Raevskii, K. S.; Likhosherstov, A. M.; Stavrovskaya, A. V.

PATENT ASSIGNEE(S): Ger. Dem. Rep.

SOURCE: Ger. (East), 30 pp.

CODEN: GEXXA8

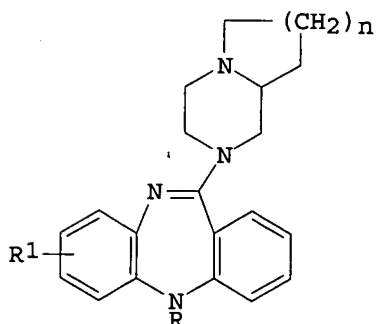
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 151166	Z	19811008	DD 1979-216678	19791105
PRIORITY APPLN. INFO.: GI			DD 1979-216678	19791105



I

AB Dibenzazepines I (R = H, Me; R1 = H, Cl; n = 1-3) were prepd. Thus 8-chloro-10,11-dihydro-11-oxo-5H-dibenzo[b,e][1,4]diazepine was treated with octahydropyrrolo[1,2-a]pyrazine to give 58% I (R = H, R1 = 8-Cl, n = 1) which had a spontaneous motility-inhibiting ED50 of 3.9 mg/kg in mice.

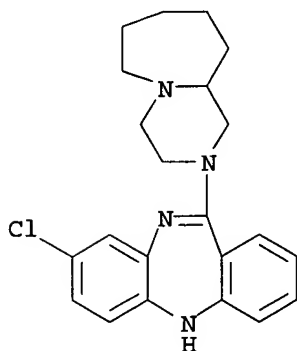
IT 81469-87-6P 81469-88-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

10/ 068,114

RN 81469-87-6 CAPLUS

CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl) - (9CI) (CA INDEX NAME)



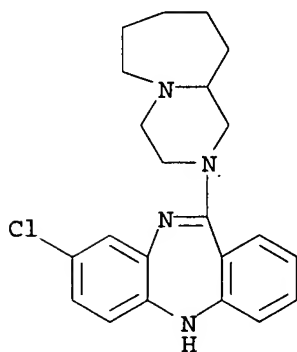
RN 81469-88-7 CAPLUS

CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 81469-87-6

CMF C22 H25 Cl N4

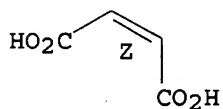


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



L4 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

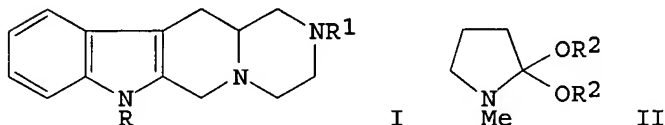
ACCESSION NUMBER: 1981:532811 CAPLUS

DOCUMENT NUMBER: 95:132811

TITLE: A convenient method for indole N-alkylation in substituted pyrazino[2,1:6,1]pyrido[3,4-b]indoles

10/ 068,114

AUTHOR(S): Agarwal, Shiv K.; Saxena, Anil K.; Anand, Nitya
CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow,
226001, India
SOURCE: Synthesis (1981), (6), 465-6
CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



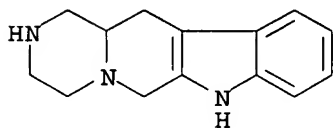
AB Treatment of pyrazinopyridoindoles I [R = H; R1 = PhCH2, 2-(4-pyridyl)ethyl, 4-FC6H4CO(CH2)3, 4-ClC6H4CONHCH2CH2] with dialkoxypyrrolidines II (R2 = Me, Et, Pr) in THF at 35.degree. for 6 h gave 72-90% I (R = Me, Et, Pr; R1 as above).

IT 55344-28-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(benzylation of)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)

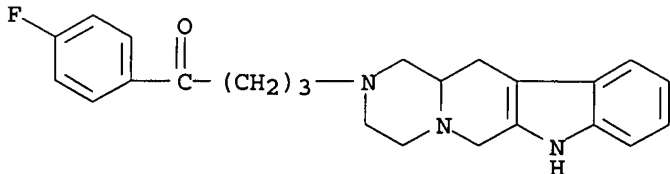


IT 42021-34-1P 55344-34-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and alkylation of, by dialkoxypyrrolidines)

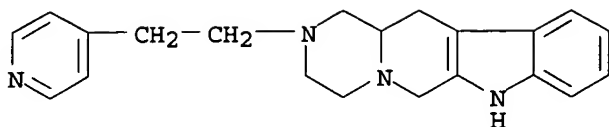
RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

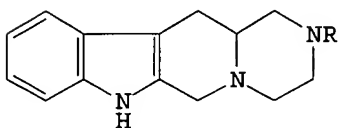


RN 55344-34-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1981:208809 CAPLUS
 DOCUMENT NUMBER: 94:208809
 TITLE: Agents acting on CNS. Part XXX. Synthesis of
 2-substituted 1,2,3,4,6,7,12,12a-
 octahydropyrazino[2'1':6,1]pyrido[3,4b]indoles
 AUTHOR(S): Dhaon, Madhup K.; Kumar, Naresh; Agarwal, Shiv K.;
 Saxena, Anil K.; Jain, Padam C.; Anand, Nitya
 CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India
 SOURCE: Indian Journal of Chemistry, Section B: Organic
 Chemistry Including Medicinal Chemistry (1980),
 19B(10), 882-5
 CODEN: IJSBDB; ISSN: 0376-4699
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



I

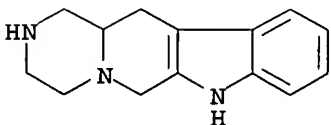
AB 2-Substituted pyrazinopyridoindoles I [R = p-ClC₆H₄CO,
 p-FC₆H₄CMe(OH)(CH₂)₃, Ph₂C:CHCH₂, etc.] were prepd. by the condensation of
 I (R = H) with the appropriate halogen compds. Treatment of I (R = H)
 with ethylene oxide gives I (R = HOCH₂CH₂) which on condensation with
 p-fluorobenzoyl chloride yields I (R = p-FC₆H₄CO₂CH₂CH₂). The
 corresponding 2- γ -(p-fluorobenzoyl)propyl-6-
 oxooctahydropyrazinopyridoindole is prepd. by the oxidn. of I (R = H) with
 mercuric acetate followed by condensation of the resulting 6-oxo deriv.
 with γ -chloro-p-fluorobutyrophenone. 2-Substituted-1-
 oxopyrazinopyridoindoles are prepd. by the reaction of ethylene oxide with
 Me 1,2,3,4-tetrahydropyrido[3,4-b]indole-3-carboxylate followed by
 condensation of the resulting oxazino deriv. with amines. These compds.
 show tranquilizing, antiinflammatory, and diuretic activities.

IT 55344-28-0

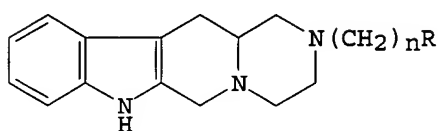
RL: RCT (Reactant); RACT (Reactant or reagent)
 (substitution reactions of)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
 (9CI) (CA INDEX NAME)



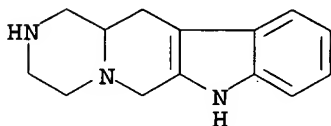
L4 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1980:69309 CAPLUS
 DOCUMENT NUMBER: 92:69309
 TITLE: Antihistaminic activity of 2-substituted
 pyrazinopyridoindoles
 AUTHOR(S): Patnaik, G. K.; Jain, P. C.; Das, P. K.; Dhawan, B. N.
 CORPORATE SOURCE: Dep. Pharmacol., Inst. Med. Sci., Lucknow, India
 SOURCE: Indian Journal of Pharmacology (1979), 11(2), 139-42
 CODEN: INJPD2; ISSN: 0253-7613
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB The relative antihistaminic activities of 39 pyrazinopyridoindoles I (R = substituted benzamido, OCHPhC₆H₄F-4, etc; n = 2 or 3) were tested in isolated guinea pig ileum preps. and were related to structure. All of the compds. selectively blocked the response of the ileum to histamine-2HCl without affecting acetylcholine chloride-induced spasms. Even the most active of the derivs. were 10-fold less effective than the ref. std. diphenhydroamine.

IT 55344-28-0D, derivs.
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antihistaminic activity of, structure in relation to)

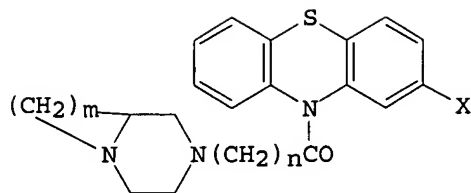
RN 55344-28-0 CAPLUS
 CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-(9CI) (CA INDEX NAME)



L4 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1978:590804 CAPLUS
 DOCUMENT NUMBER: 89:190804
 TITLE: Azacycloalkanes. XXI. Relation between the structure and the antianginal properties in a series of 1,4-diazabicyclo[4.m.0]alkanyl derivatives of 10-acylphenothiazines
 AUTHOR(S): Nazarova, L. S.; Likhosherstov, A. M.; Markova, G. A.; Chichkanov, G. G.; Kaverina, N. V.; Skoldinov, A. P.
 CORPORATE SOURCE: Inst. Farmakol., Moscow, USSR
 SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1978), 12(6), 84-9
 CODEN: KHFZAN; ISSN: 0023-1134
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian

10/ 068,114

GI



AB The title compds (I) ($n = 1, 2$, or 3 ; $m = 3$ or 5 ; $X = H$, Cl , or CF_3) were prepd. by condensation of 1,4-diazobicyclo[4.m.0]alkanes with 10-(ω -chloroacyl)phenothiazines and studied for their effects on coronary blood flow and myocardial function in cats. Lengthening of the acyl group increased coronary blood flow and increased myocardial contraction without the development of tachycardia. Trichloromethyl substitution at position 2 of the phenothiazine system increased the duration of coronary blood flow effects. The 1,4-diazabicyclo[4.5.0] derivs. were less active than the 1,4-diazabicyclo[4.3.0] derivs. The most promising antianginal compds. were 10- β -N-(1,4-diazabicyclo[4.3.0]nonaryl)propionyl]-2-chlorophenothiazine dihydrochloride [49780-10-1] and 10- β -N-(1,4-diazabicyclo[4.3.0]nonanyl)propionyl]-2-trifluoromethylphenothiazine dihydrochloride [49780-09-8].

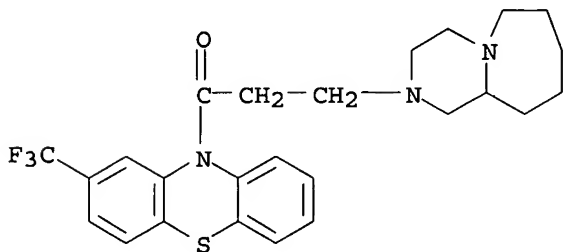
IT 49780-15-6 68027-97-4

RL: BIOL (Biological study)

(antianginal properties of, structure in relation to)

RN 49780-15-6 CAPLUS

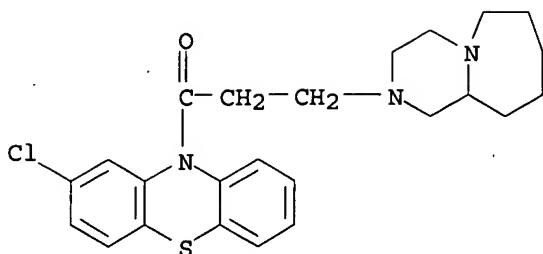
CN 10H-Phenothiazine, 10-[3-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-1-oxopropyl]-2-(trifluoromethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 68027-97-4 CAPLUS

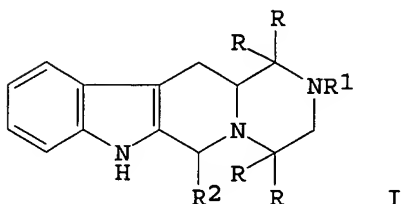
CN 10H-Phenothiazine, 2-chloro-10-[3-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-1-oxopropyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L4 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1977:171497 CAPLUS
 DOCUMENT NUMBER: 86:171497
 TITLE: Tetracyclic compounds
 PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India),
 India
 SOURCE: Brit., 9 pp.
 CODEN: BRXXAA
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1454171	A	19761027	GB 1973-44002	19731019
PRIORITY APPLN. INFO.: GI			GB 1973-44002	19731019



AB Thirty-one 2-substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-b]indoles I [R = H, R2 = O; R1 = aroylalkyl, arylhydroxyalkyl, hydroxyalkyl, oxoalkyl, aminoalkyl, Me, PhCH2CO, Ph(CH2)2, benzodioxanylmethyl, PhOCH(OH)CH2, NC(CH2)2, HO2C(CH2)2, EtO2C(CH2)2; R2 = H, Me] were prep'd. from alkyl 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylates by 2 main methods. The 1st involved successive acid-catalyzed condensation with ethylenimine (II), (if necessary) LiAlH4 redn., and introduction of 2-substituents. The 2nd involved successive treatment with haloacetyl halides and primary amines. Thus, I [R = R2 = H, R1 = p-FC6H4CO(CH2)3] (III) was prep'd. from Me 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylate (IV) by refluxing with IV.HCl and II in EtOH 48 h followed by LiAlH4 redn. in THF and treatment with p-FC6H4CO(CH2)3Cl in DMF contg. Na2CO3 and NaI 36 h at 80.degree.. I show strong tranquilizing and hypotensive activity. Animal tests on III are reported; III had LD50 values in mice of 180 mg/kg i.p. and >1 g orally. III also shows antiemetic activity.

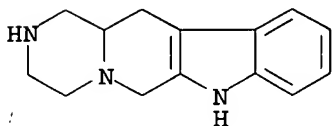
10/ 068,114

IT 55344-28-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and alkylation of)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)

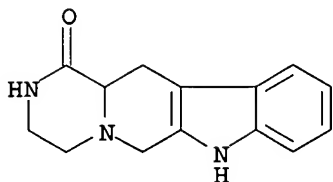


IT 55344-27-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and redn. of)

RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro-
(9CI) (CA INDEX NAME)

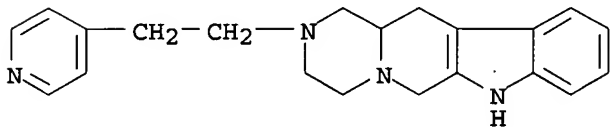


IT 55344-34-8P 55344-36-0P 55344-50-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(tranquilizers and hypotensive agent, prepn. of)

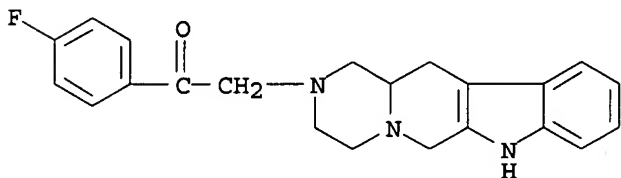
RN 55344-34-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-
(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



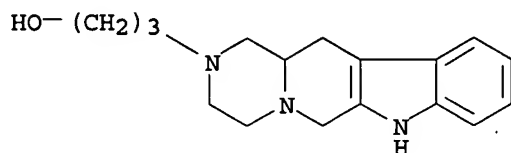
RN 55344-36-0 CAPLUS

CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

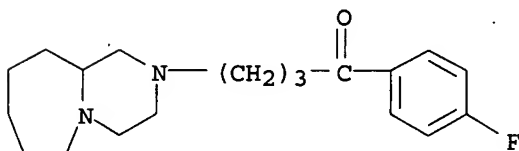


10/ 068,114

RN 55344-50-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol,
3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)

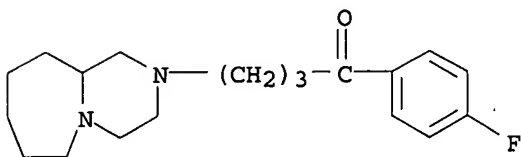


L4 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:508620 CAPLUS
DOCUMENT NUMBER: 85:108620
TITLE: Azacycloalkanes. XV. Relation between the structure and neurotropic activity in a series of 1,4-diazabicyclo[4.m.0]alkanyl derivatives of butyrophenone
AUTHOR(S): Nazarova, L. S.; Likhosherstov, A. M.; Raevskii, K. S.; Breger, M. A.; Skoldinov, A. P.
CORPORATE SOURCE: Inst. Farmakol., Moscow, USSR
SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1976), 10(4), 49-55
CODEN: KHFZAN; ISSN: 0023-1134
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB Five diazabicycloalkanes I (m = 3, 4, 5; X = F, Cl, H) were prepd. in 31-62.9% yield by reaction of the corresponding diazabicycloalkanes with X1(CH₂)₃COC₆H₄X-p (X₁ = Cl, Br); the dihydrochlorides were also prepd. Redn. of I (m = 3; X = F) gave 74% resp. alc. Reaction of 1,4-diazabicyclo[4.3.0]nonane-4-ethanol with p-XC₆H₄COCl (X = H, F) gave the corresponding II in 58.7 and 38% yield, resp. 1,4-Diazabicyclo[4.3.0]nonane-4-butyric acid was prepd. in 66.5% yield by hydrolysis of the Et ester. I (m = 4, X = F) increased the duration of the narcotic effect of sodium thiopental and was more active than I (m = 3, 5, X = F). When X = F the compds. had a stronger neuroleptic effect than when X = Cl, H. The CO played an important role in neuroleptic activity.
IT 60390-52-5P
RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and neurotropic activity of)
RN 60390-52-5 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)- (9CI) (CA INDEX NAME)



IT 60417-35-8P
RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
RN 60417-35-8 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L4 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1976:405673 CAPLUS

DOCUMENT NUMBER: 85:5673

TITLE: 2-Substituted-1,2,3,4,6,7,12,12a-octahydropyrazino-[2',1':6,1]pyrido[3,4-b]indoles

INVENTOR(S): Saxena, Anil K.; Jain, Padam C.; Dua, Prithvi R.; Srimal, Rikhab C.; Dhawan, Bhola N.; Anand, Nitya; Singh, Gurbuksh

PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India), India

SOURCE: Can., 25 pp.
CODEN: CAXXA4

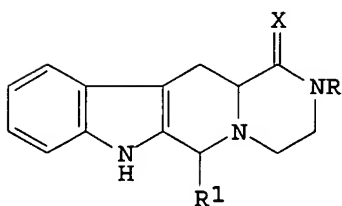
DOCUMENT TYPE: Patent

LANGUAGE: English

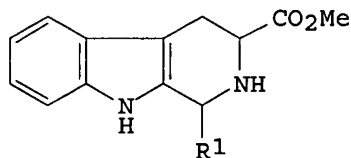
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 982132	A1	19760120	CA 1973-172016	19730523
PRIORITY APPLN. INFO.: GI			CA 1973-172016	19730523



I



II

AB About 30 pyrazinopyridoindoles I (R = H, p-FC6H4CO(CH2)3, Me, 2-(4-pyridyl)ethyl, Et2NCH2CH2, PhCH2CO, EtO2CCH2CH2, MeCOCH2CH2, etc.; R1 = H, Me; X = H2) were prepd. from II. Thus II (R1 = H) was treated with ethylenimine and the I (R = R1 = H, X = O) reduced with LiAlH4 to give I (R = R1 = H, X = H2), which was treated with Cl(CH2)3COC6H4F-p to give I [R = p-FC6H4CO(CH2)3, R1 = H, X = H2] (III). The depressant ED50 of III was 0.5 mg/kg in the amphetamine hyperactivity test (i.p. mice).

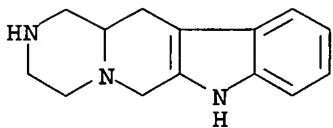
IT 55344-28-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of)

RN 55344-28-0 CAPLUS

10/ 068,114

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)

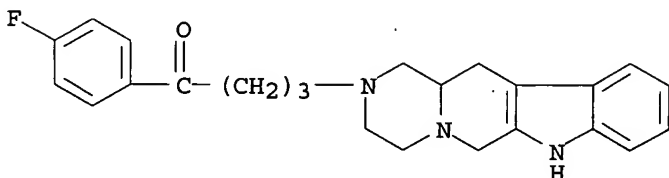


IT 42021-34-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and depressant activity of)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

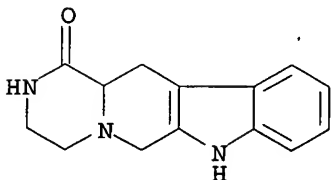


IT 55344-27-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)

RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro-
(9CI) (CA INDEX NAME)

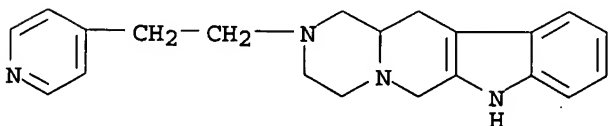


IT 55344-34-8P 55344-36-0P 55344-50-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

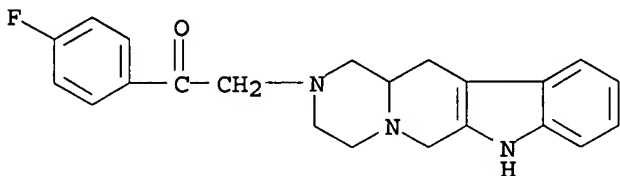
RN 55344-34-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

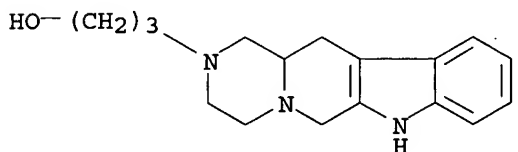


10/ 068,114

RN 55344-36-0 CAPLUS
CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

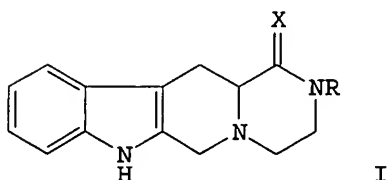


RN 55344-50-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:164842 CAPLUS
DOCUMENT NUMBER: 84:164842
TITLE: 2-Substituted-1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indoles
INVENTOR(S): Saxena, Anil K.; Jain, Padam C.; Singh, Gurbuksh; Dua, Prithvi R.; Srimal, Rikhab C.; Dhawan, Bhola N.; Anand, Nitya
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India), India
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3917599	A	19751104	US 1973-346468	19730330
PRIORITY APPLN. INFO.: GI			US 1973-346468	19730330



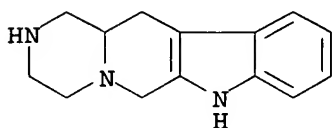
AB Me 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylate was cyclized with ethylenimine to give the pyrazinopyridoindole I (R = H, X = O), which was reduced and alkylated to give I (R = Me. PhCH₂CO, p-FC₆H₄CO(CH₂)₃, 4-pyridylethyl, etc., X = H₂). At 2.5-35 mg/kg I [R = p-FC₆H₄CO(CH₂)₃, X = H₂] (II) reduced spontaneous motor activity of mice in several tests. The LD₅₀ of II was 180 mg/kg, i.p. in mice.

IT 55344-28-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-(9CI) (CA INDEX NAME)

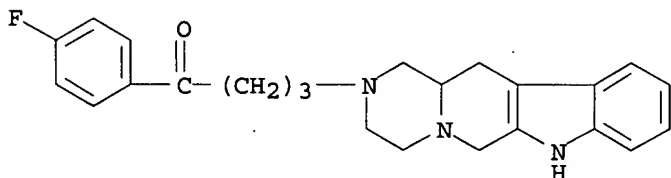


IT 42021-34-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and depressant activity of)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)-(9CI) (CA INDEX NAME)

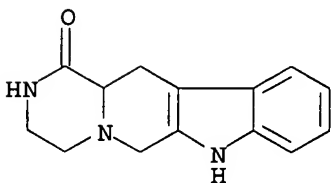


IT 55344-27-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)

RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro-(9CI) (CA INDEX NAME)



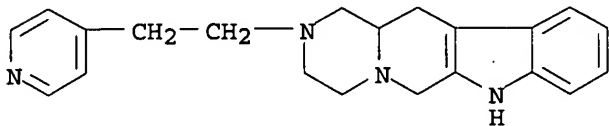
IT 55344-34-8P 55344-36-0P 55344-50-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 55344-34-8 CAPLUS

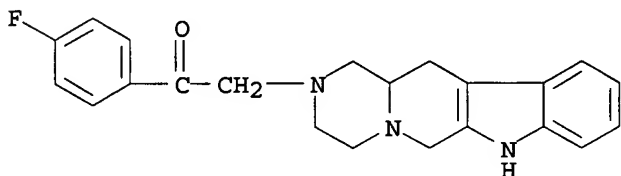
10/ 068,114

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



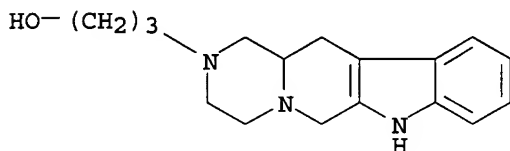
RN 55344-36-0 CAPLUS

CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



RN 55344-50-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1975:171057 CAPLUS

DOCUMENT NUMBER: 82:171057

TITLE: 1,2,3,4,6,7,12,12a-Octahydropyrazino[2,1:6,1]pyrido[3,4-b]indole depressants

INVENTOR(S): Saxena, Anil K.; Jain, Padam C.; Singh, Gurbukhsh; Dua, Prithvi R.; Srimal, Rikhab C.; Dhawan, Bhola N.; Anand, Nitya

PATENT ASSIGNEE(S): Gruppo Lepetit S.p.A.

SOURCE: Fr. Demande, 16 pp.

CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
FR 2223013	A1	19741025	FR 1974-9968	19740322
FR 2223013	B1	19770701		
SE 408710	C	19791011	SE 1973-14117	19731017
SE 408710	B	19790702		
AU 7361649	A1	19750424	AU 1973-61649	19731022

NL 171270	B	19821001	NL 1973-15803	19731119
NL 171270	C	19830301		
CH 596205	A	19780315	CH 1973-16535	19731123
DK 141702	B	19800527	DK 1974-1712	19740328
DK 141702	C	19801027		

PRIORITY APPLN. INFO.: US 1973-346408 19730330

GI For diagram(s), see printed CA Issue.

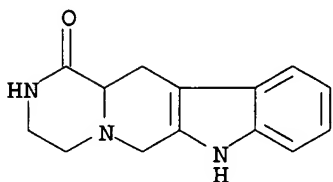
AB Pyrazinopyridoindoles I (R = oxoalkyl, hydroxyalkyl, aminoalkyl etc; X = H₂, O; R₁ = H, Me) (34 compds.) were prepd. for use as central nervous system depressants. Thus Me 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylate was treated with ethylenimine and reduced with LiAlH₄ to give I (X = H₂, R = R₂ = H), which was treated with p-FC₆H₄CO(CH₂)₃Cl to give I (X = H₂, R = (CH₂)₃COC₆H₄F-4, R₁ = H). The latter compd. had a ED₅₀ in the Rotarod test in mice of 5.9 mg/kg i.p.

IT 55344-27-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)

RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro-(9CI) (CA INDEX NAME)

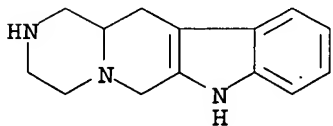


IT 55344-28-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and substitution reactions of)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-(9CI) (CA INDEX NAME)

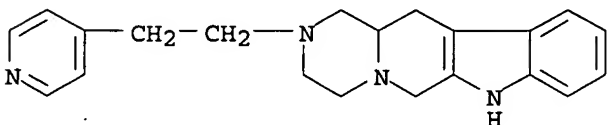


IT 55344-34-8P 55344-36-0P 55344-50-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 55344-34-8 CAPLUS

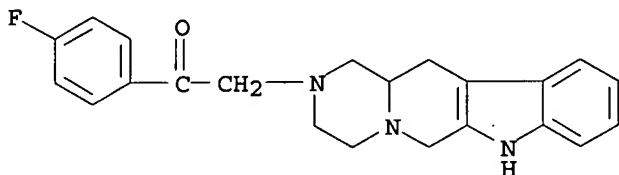
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



10/ 068,114

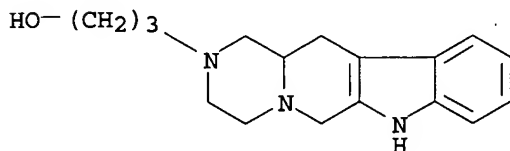
RN 55344-36-0 CAPLUS

CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl) - (9CI) (CA INDEX NAME)



RN 55344-50-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)

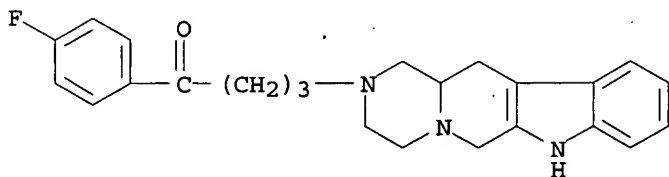


IT 42021-34-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., redn., and central depressant activity of)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl) - (9CI) (CA INDEX NAME)



L4 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1975:156373 CAPLUS

DOCUMENT NUMBER: 82:156373

TITLE: 2-Substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-d]indole

INVENTOR(S): Saxena, Anil K.; Jain, Padam C.; Singh, Gurbakhsh; Dua, Fritzvi R.; Srimal, Rikhab C.; Dhawan, Bhola N.; Anand, Nitya

PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India)

SOURCE: Ger. Offen., 21 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2333922	A1	19750130	DE 1973-2333922	19730704

PRIORITY APPLN. INFO.: DE 1973-2333922 19730704

GI For diagram(s), see printed CA Issue.

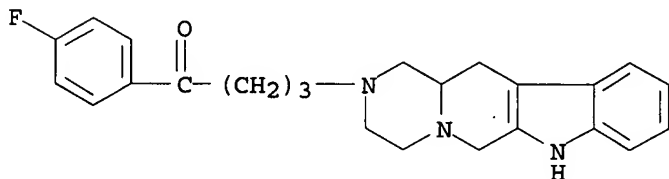
AB Approx. 30 central nervous system depressants (I, R1 = e.g., H, Me, CH₂CH₂Ph, 4-pyridylethyl, CH₂COC₆H₄F-p; R2 = H, Me; Y, Z = O, H₂) were prepd. via cycloaddn. of II with ethylenimine (III) or ClCH₂COC₆H₄F and amines followed by redn. with LiAlH₄. Thus, II was refluxed with III in EtOH for 24 hr to give I (R1 = R2 = H, Y = O, Z = H₂) which was reduced with LiAlH₄ in refluxing THF for 48 hr and treated with p-FC₆H₄CO(CH₂)₃Cl to yield I [R1 = (CH₂)₃COC₆H₄F-p, R3 = H, Y = Z = H₂] (IV). IV has i.p. LD₅₀ = 180 mg/kg in mice and orally LD₅₀ = 700 mg/kg in rats.

IT 42021-34-1P 55344-34-8P 55344-36-0P
55344-50-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(depressant, prepn. of)

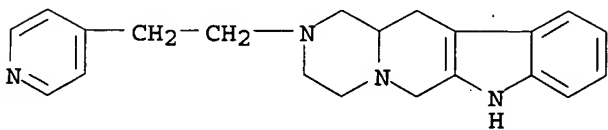
RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



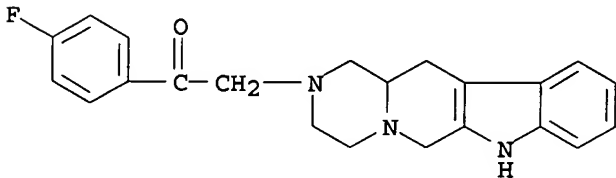
RN 55344-34-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME).



RN 55344-36-0 CAPLUS

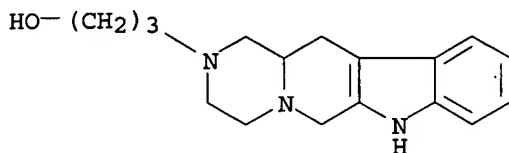
CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



RN 55344-50-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)

10/ 068,114

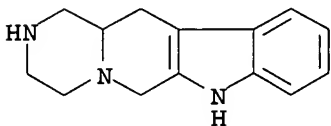


IT 55344-28-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and reactions of)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)

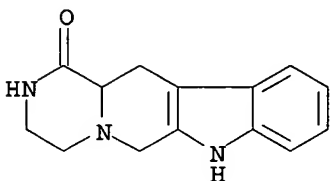


IT 55344-27-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and redn. of)

RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro-
(9CI) (CA INDEX NAME)



L4 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1974:83008 CAPLUS

DOCUMENT NUMBER: 80:83008

TITLE: 10-[.omega.-N-(1,4-Diazabicycloalkanyl)acyl]phenothiaz
ines

INVENTOR(S): Likhosherstov, A. M.; Nazarova, L. S.; Skoldinov, A.
P.; Markova, G. A.; Kaverina, N. V.

PATENT ASSIGNEE(S): Institute of Pharmacology, Academy of Medical
Sciences, U.S.S.R.

SOURCE: Brit., 6 pp.
CODEN: BRXXAA

DOCUMENT TYPE: Patent

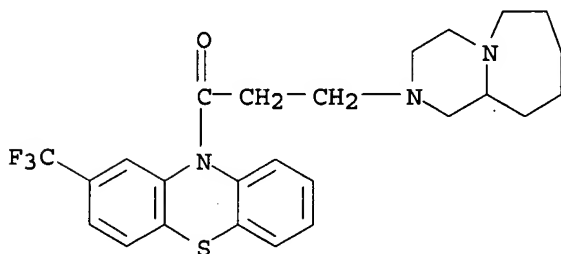
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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GB 1338363 A 19731121 GB 1972-10593 19720307
 PRIORITY APPLN. INFO.: GB 1972-10593 19720307
 GI For diagram(s), see printed CA Issue.
 AB Six title compds. (I; m = 3,5; n = 1-3; R = H, Cl, CF₃) and/or their acid addn. salts and methiodides, useful as coronary-dilatants and spasmolytics, were prepd. by condensing (.omega.-chloroacyl)phenothiazines with 1,4 - diazabicycloalkanes. Thus, refluxing 7.2 g 10-(.beta.-chloropropionyl)-2-(trifluoromethyl)phenothiazine with 5.04 g 1,4-diazabicyclo[4.3.0]nonane in PhMe for 3 hr gave 7.35 g I.2HCl (m = 3, n = 2, R = CF₃). The results of clinical tests with I.2HCl (m = 3, n = 2, R = Cl) were reported.
 IT **49780-15-6P**
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
 RN 49780-15-6 CAPLUS
 CN 10H-Phenothiazine, 10-[3-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-1-oxopropyl]-2-(trifluoromethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L4 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1973:526514 CAPLUS
 DOCUMENT NUMBER: 79:126514
 TITLE: Coronary dilating 10-[.omega.-(1,4-diazabicycloalk-4-yl)acyl]phenothiazines
 INVENTOR(S): Likhosherstov, A. M.; Nazarova, L. S.; Skoldinov, A. P.; Markova, G. A.; Kaverina, N. V.
 PATENT ASSIGNEE(S): Scientific-Research Institute of Pharmacology and Chemotherapy, Academy of Medical Sciences, U.S.S.R.
 SOURCE: Ger. Offen., 18 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2210382	A1	19730906	DE 1972-2210382	19720303
DE 2210382	C2	19820603		

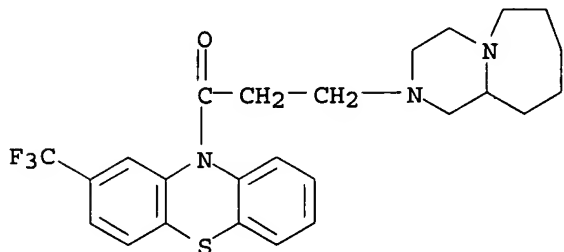
PRIORITY APPLN. INFO.: DE 1972-2210382 19720303
 GI For diagram(s), see printed CA Issue.
 AB Twelve phenothiazines I (R = H, Cl, or CF₃; n = 1-3, m = 3 or 5) or their salts were prepd. by reaction of II with 1,4-diazabicyclo[4.m.0]alkanes in an org. solvent at 50-140.degree. and were effective as coronary dilating pharmaceuticals.
 IT **49780-15-6P**
 RL: SPN (Synthetic preparation); PREP (Preparation)

10/ 068,114

(prepn. of)

RN 49780-15-6 CAPLUS

CN 10H-Phenothiazine, 10-[3-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-1-oxopropyl]-2-(trifluoromethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L4 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1973:461395 CAPLUS

DOCUMENT NUMBER: 79:61395

TITLE: Agents acting on the central nervous system. 15.
2-Substituted 1,2,3,4,6,7,12,12a-octahydropyrazino
[2',1':6,1]pyrido[3,4-b]indoles. New class of central
nervous system depressants

AUTHOR(S): Saxena, Anil K.; Jain, Padam C.; Anand, Nitya; Dua, P.
R.

CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, India

SOURCE: Journal of Medicinal Chemistry (1973), 16(5), 560-4

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2-[4-(4-Fluorophenyl)-4-oxobutyl]-1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indole (I) [41510-23-0] and related compds. showed depressant properties in rats and mice. I produced 60% inhibition of amphetamine-induced hyperactivity in mice at 0.6 mg/kg i.p., decreased forced motor activity in mice by 50% at 7.5 mg/kg i.p., produced 50% inhibition of conditioned avoidance responses in rats at 0.15 mg/kg i.p., and counteracted amphetamine toxicity in mice by 50% at 3.5 mg/kg i.p., and was thus more potent than chlorpromazine. 2-[4-(4-Fluorophenyl)-4-hydroxybutyl]-1,2,3,4,6,7,12,12a-octahydropyrazinol[2',1':6,1]pyrido[3,4-b]indole [41510-24-1], and 2-(3-hydroxybutyl)-1,2,3,4,6,7,12,12a-octa-hydropyrazino[2',1':6,1]pyrido[3,4-b]indole [41510-25-2] were also highly active depressants. I was prepd. by converting the known dl-1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylic acid [41509-88-0] to the Me ester, reacting with ethyleneimine [151-56-4] to yield dl-1-oxo-1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indole [41509-89-1], reducing the keto group with LiAlH₄, and reacting at N-2 with the appropriate chloride.

IT 42021-23-8P 42021-34-1P 55344-34-8P

55344-36-0P 55344-50-8P

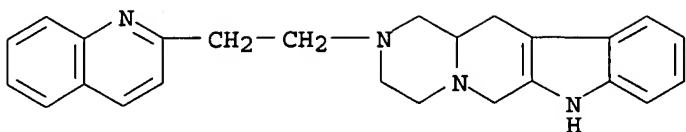
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and central nervous system depressant activity of)

RN 42021-23-8 CAPLUS

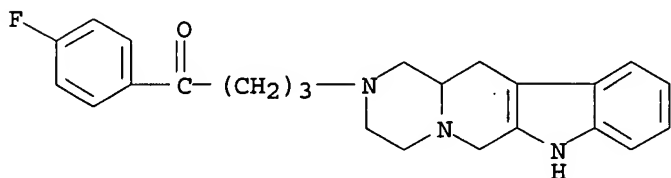
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(2-quinolinyl)ethyl]- (9CI) (CA INDEX NAME)

10/.068,114



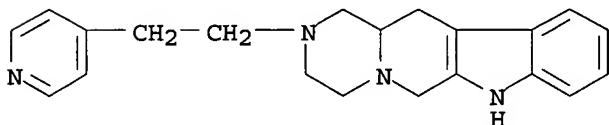
RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl) - (9CI) (CA INDEX NAME)



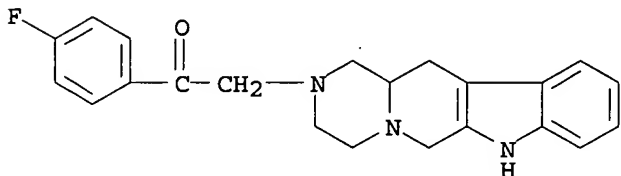
RN 55344-34-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



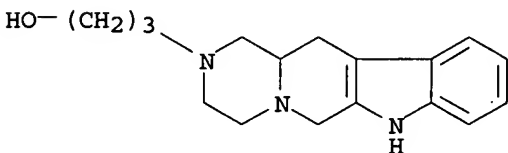
RN 55344-36-0 CAPLUS

CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl) - (9CI) (CA INDEX NAME)



RN 55344-50-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



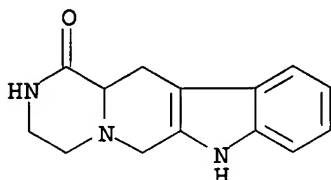
IT 55344-27-9P 55344-28-0P

10/ 068,114

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

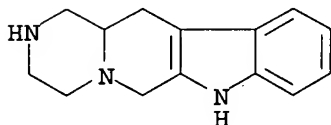
RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro-
(9CI) (CA INDEX NAME)



RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)



=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

183.11

336.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

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-26.04

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NEWS	3	Feb 24	PCTGEN now available on STN
NEWS	4	Feb 24	TEMA now available on STN
NEWS	5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS	6	Feb 26	PCTFULL now contains images
NEWS	7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS	8	Mar 24	PATDPAFULL now available on STN
NEWS	9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS	10	Apr 11	Display formats in DGENE enhanced
NEWS	11	Apr 14	MEDLINE Reload
NEWS	12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS	13	SEP 09	CA/CAPLUS records now contain indexing from 1907 to the present
NEWS	14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS	15	Apr 28	RDISCLOSURE now available on STN
NEWS	16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS	17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS	18	May 15	Supporter information for ENCOMPAT and ENCOMPLIT updated
NEWS	19	May 19	Simultaneous left and right truncation added to WSCA
NEWS	20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS	21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS	22	Jun 06	PASCAL enhanced with additional data
NEWS	23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS	24	Jun 25	HSDB has been reloaded
NEWS	25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS	26	Jul 21	Identification of STN records implemented
NEWS	27	Jul 21	Polymer class term count added to REGISTRY
NEWS	28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS	29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS	30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS	31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS	32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS	33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS	34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS	35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS	36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS	37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation
NEWS	38	AUG 18	Simultaneous left and right truncation added to ANABSTR

10/ 068,114

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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FILE 'HOME' ENTERED AT 07:51:19 ON 11 SEP 2003

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 07:51:28 ON 11 SEP 2003

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STRUCTURE FILE UPDATES: 9 SEP 2003 HIGHEST RN 582289-61-0
DICTIONARY FILE UPDATES: 9 SEP 2003 HIGHEST RN 582289-61-0

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when
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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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Uploading 10068114.str

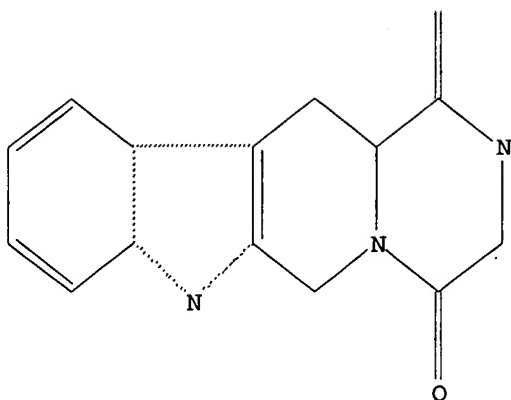
L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

10/ 068,114



Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful

FULL SEARCH INITIATED 07:51:50 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 292 TO ITERATE

100.0% PROCESSED 292 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

L2 0 SEA SSS FUL L1

=> s 'dioxo pyrazino'

516187 'DIOXO'

17300 'PYRAZINO'

L3 56 'DIOXO PYRAZINO'

('DIOXO' (W) 'PYRAZINO')

=> d scan l3

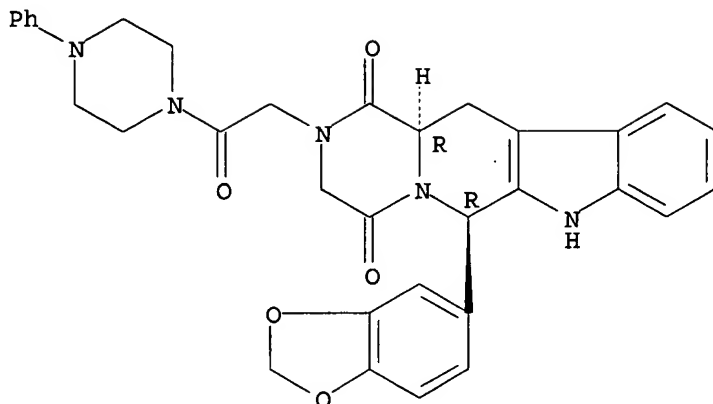
L3 56 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN

IN Piperazine, 1-[[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]-4-phenyl- (9CI)

MF C33 H31 N5 O5

Absolute stereochemistry.

10/ 068,114



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

157.39

157.60

FILE 'CAPLUS' ENTERED AT 07:53:17 ON 11 SEP 2003

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FILE COVERS 1907 - 11 Sep 2003 VOL 139 ISS 11

FILE LAST UPDATED: 10 Sep 2003 (20030910/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4

24 L3

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YOU HAVE REQUESTED DATA FROM 24 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

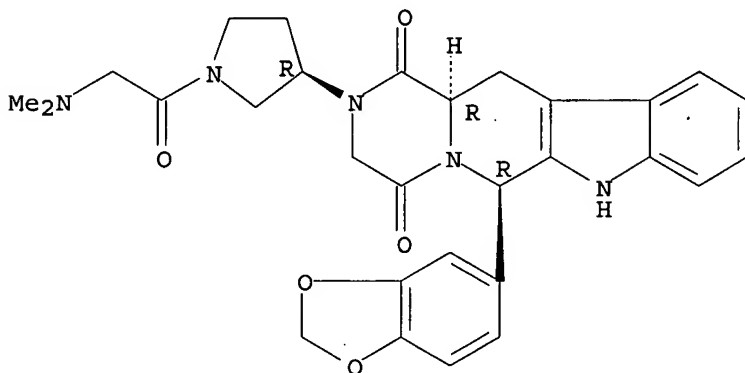
ACCESSION NUMBER: 2003:262948 CAPLUS

DOCUMENT NUMBER: 139:159439

TITLE: Design, synthesis and biological activity of .beta.-carboline-based type-5 phosphodiesterase

inhibitors
 AUTHOR(S): Maw, Graham N.; Allerton, Charlotte M. N.; Gbekor, Eugene; Million, William A.
 CORPORATE SOURCE: Pfizer Global Research and Development, Department of Discovery Chemistry, Sandwich Laboratories (IPC351), Sandwich, Kent, CT13 9NJ, UK
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(8), 1425-1428
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The SAR of a series of .beta.-carboline derived type 5 phosphodiesterase inhibitors has been explored and we have discovered compds. with excellent levels of PDE5 potency and selectivity over PDE6. However, the series exhibits low levels of selectivity over PDE11, a phosphodiesterase with unknown function.
 IT 574730-13-5P 574730-14-6P 574730-15-7P
 574730-16-8P 574730-17-9P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (design, synthesis and structure-activity relationship of .beta.-carboline-based type-5 phosphodiesterase inhibitors)
 RN 574730-13-5 CAPLUS
 CN Pyrrolidine, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-1-[(dimethylamino)acetyl]-, (3R)- (9CI) (CA INDEX NAME)

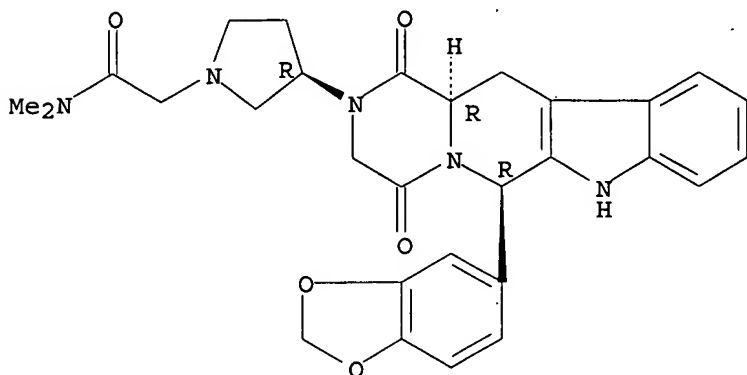
Absolute stereochemistry.



RN 574730-14-6 CAPLUS
 CN 1-Pyrrolidineacetamide, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-N,N-dimethyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

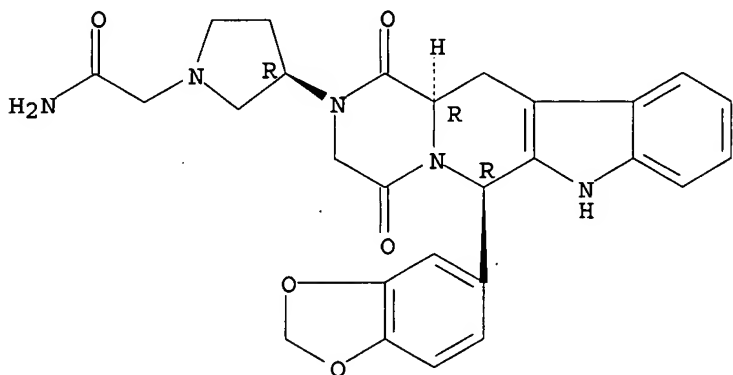
10/ 068,114



RN 574730-15-7 CAPLUS

CN 1-Pyrrolidineacetamide, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-, (3R)-(9CI) (CA INDEX NAME)

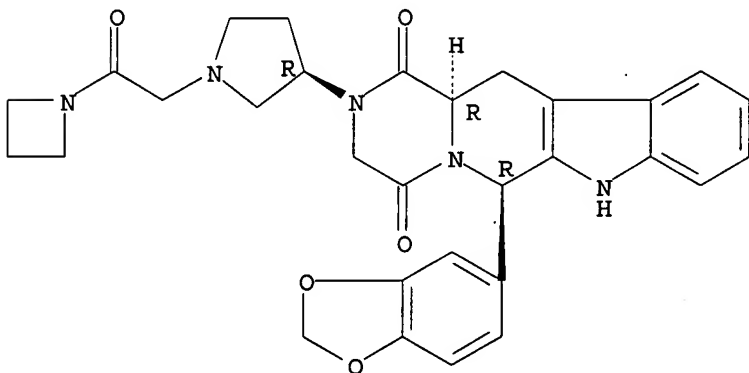
Absolute stereochemistry.



RN 574730-16-8 CAPLUS

CN Azetidine, 1-[(3R)-3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-1-pyrrolidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



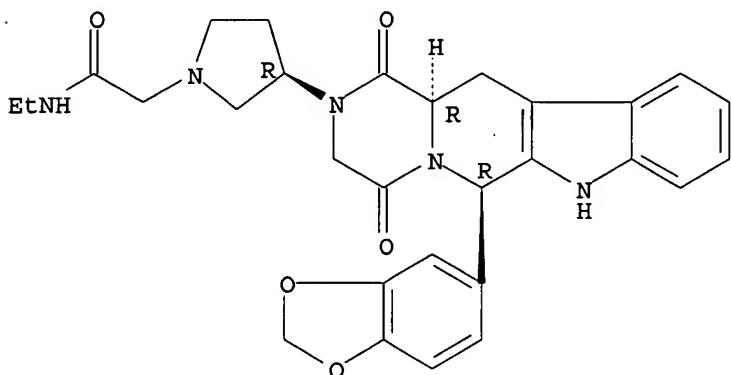
RN 574730-17-9 CAPLUS

CN 1-Pyrrolidineacetamide, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-

10/ 068,114

2 (1H) -yl] -N-ethyl-, (3R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:714162 CAPLUS

DOCUMENT NUMBER: 137:232664

TITLE: Preparation of pyrazolopyrimidines as inhibitors of guanosine 3',5'-monophosphate phosphodiesterases (cGMP PDEs).

INVENTOR(S) : Barber, Christopher Gordon; Maw, Graham Nigel

PATENT ASSIGNEE(S) : Pfizer Limited, UK; Pfizer Inc.

SOURCE: Eur. Pat. Appl., 96 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1241170	A2	20020918	EP 2002-251367	20020227
EP 1241170	A3	20030312		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2002193388 A1 20021219 US 2002-93105 20020306

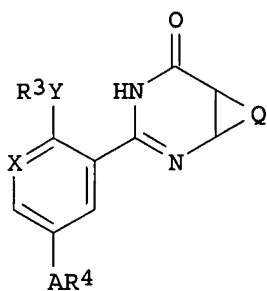
JP 2002322180 A2 20021108 JP 2002-68015 20020313

BR 2002000843 A 20030325 BR 2002-843 20020318

PRIORITY APPLN. INFO.:	GB 2001-6631	A	20010316
	US 2001-290734P	P	20010514

OTHER SOURCE(S) : MARPAT 137:232664

GI



I

AB Title compds. [I; Q = (substituted) fused pyrazolo; A = SO₂, CO, CH(OH); V = O, NR₅; X = CH, N; R₃-R₅ = H, alkyl, cycloalkyl, (substituted) heterocyclyl, aryl, etc.]; were prepd. e.g. for treatment of mammalian sexual disorders (no data). Thus, potassium bis(trimethylsilyl)amide was added to a soln. of 3-[[[2-ethoxy-5-[(4-ethyl-1-piperazinyl)sulfonyl]-3-pyridinyl]carbonyl]amino]-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazole-2-carboxamide (prepn. given) in ethanol and the reaction mixt. heated in a sealed vessel at 130.degree. for 16 h to give 2-[2-ethoxy-5-[(4-ethyl-1-piperazinyl)sulfonyl]-3-pyridinyl]-3,7,8,9-tetrahydro-4H-pyrrolo(2',1':5,1)pyrazolo[4,3-d]pyrimidin-4-one.

IT 459156-77-5P 459156-99-1P 459157-01-8P

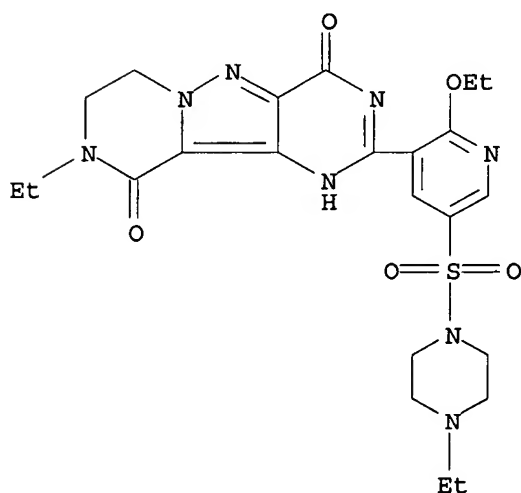
459157-03-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of pyrazolopyrimidines as inhibitors of guanosine 3',5'-monophosphate phosphodiesterases)

RN 459156-77-5 CAPLUS

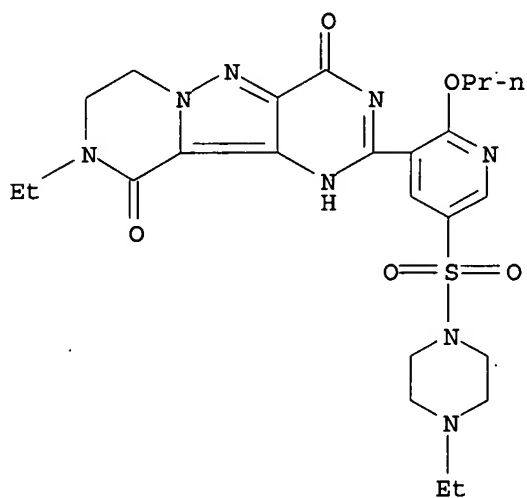
CN Piperazine, 1-[[[6-ethoxy-5-(9-ethyl-1,4,7,8,9,10-hexahydro-4,10-dioxopyrazino[1',2':1,5]pyrazolo[4,3-d]pyrimidin-2-yl)-3-pyridinyl]sulfonyl]-4-ethyl- (9CI) (CA INDEX NAME)



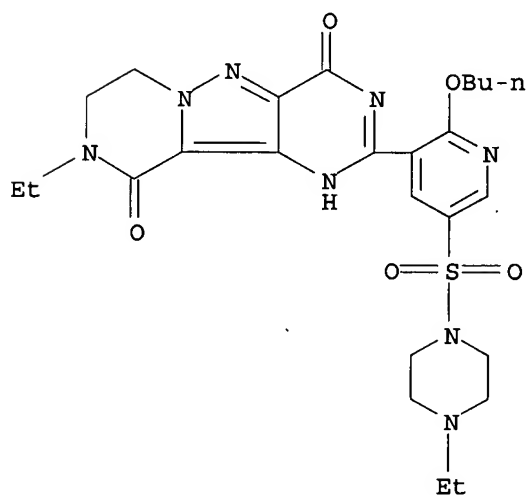
RN 459156-99-1 CAPLUS

CN Piperazine, 1-ethyl-4-[[[5-(9-ethyl-1,4,7,8,9,10-hexahydro-4,10-dioxopyrazino[1',2':1,5]pyrazolo[4,3-d]pyrimidin-2-yl)-6-propoxy-3-pyridinyl]sulfonyl]- (9CI) (CA INDEX NAME)

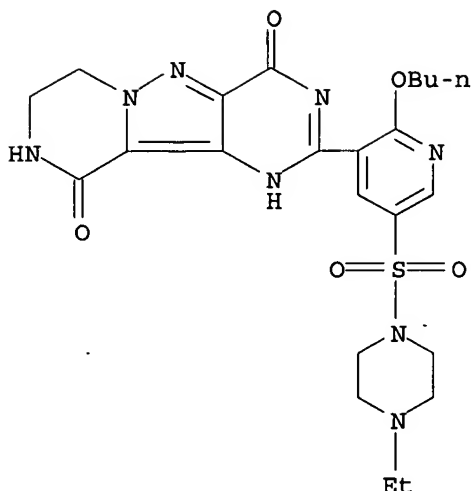
10/ 068,114



RN 459157-01-8 CAPLUS
CN Piperazine, 1-[[6-butoxy-5-(9-ethyl-1,4,7,8,9,10-hexahydro-4,10-dioxopyrazino[1',2':1,5]pyrazolo[4,3-d]pyrimidin-2-yl)-3-pyridinyl]sulfonyl]-4-ethyl- (9CI) (CA INDEX NAME)



RN 459157-03-0 CAPLUS
CN Piperazine, 1-[[6-butoxy-5-(1,4,7,8,9,10-hexahydro-4,10-dioxopyrazino[1',2':1,5]pyrazolo[4,3-d]pyrimidin-2-yl)-3-pyridinyl]sulfonyl]-4-ethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:328916 CAPLUS

DOCUMENT NUMBER: 137:241804

TITLE: Potent and specific inhibition of the breast cancer resistance protein multidrug transporter in vitro and in mouse intestine by a novel analogue of fumitremorgin C

AUTHOR(S): Allen, John D.; Van Loevezijn, Arnold; Lakhai, Jeany M.; Van der Valk, Martin; Van Tellingen, Olaf; Reid, Glen; Schellens, Jan H. M.; Koomen, Gerrit-Jan; Schinkel, Alfred H.

CORPORATE SOURCE: Division of Experimental Therapy, The Netherlands Cancer Institute, Amsterdam, 1066 CX, Neth.

SOURCE: Molecular Cancer Therapeutics (2002), 1(6), 417-425
CODEN: MCTOCF; ISSN: 1535-7163

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhibitors of the breast cancer resistance protein (BCRP/ABCG2) multidrug transporter are of interest as chemosensitizers for clin. drug resistance, for improving the pharmacokinetics of substrate chemotherapeutic drugs, and in functional assays of BCRP activity for tailoring chemotherapy. The fungal toxin fumitremorgin C (FTC) is a potent and specific inhibitor of BCRP, but its neurotoxic effects preclude use in vivo. We have therefore evaluated a new tetracyclic analog of FTC, Kol43, as a practical inhibitor of BCRP, comparing it with two other analogs in the same class and with GF120918. All three FTC analogs are effective inhibitors of both mouse Bcrp1 and human BCRP, proving highly active for increasing the intracellular drug accumulation and reversing Bcrp1/BCRP-mediated multidrug resistance. Indeed, Kol43 appears to be the most potent BCRP inhibitor known thus far. In contrast, the compds. have only low activity against P-glycoprotein, the multidrug resistance-assocd. protein (MRP1), or other known drug transporters. They are nontoxic in vitro at useful concns. and evinced no signs of toxicity in mice at high oral or i.p. doses. Administered p.o. to inhibit intestinal Bcrp1, Kol43 markedly increased the oral availability of topotecan in mice. It is thus the first highly potent and specific BCRP inhibitor applicable in vivo. As such, Kol43 and other FTC analogs of this type represent valuable reagents for anal. of drug resistance mechanisms and may be candidates for development as clin. BCRP inhibitors.

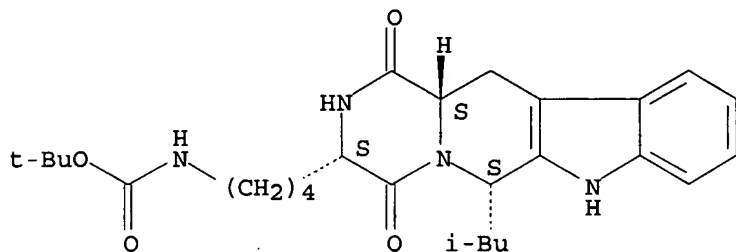
IT 329356-42-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(inhibition of breast cancer resistance protein multidrug transporter
in vitro and in mouse intestine by an analog of fumitremorgin C)

RN 329356-42-5 CAPLUS

CN Carbamic acid, [4-[(3S,6S,12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl)butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:107344 CAPLUS

DOCUMENT NUMBER: 136:151441

TITLE: Preparation of fused heterocyclic derivatives as phosphodiesterase inhibitors

INVENTOR(S): Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.

PATENT ASSIGNEE(S): Lilly Icos L.L.C., USA

SOURCE: PCT Int. Appl., 105 pp.

CODEN: PIXXD2

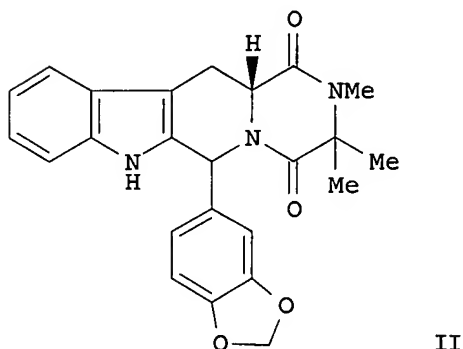
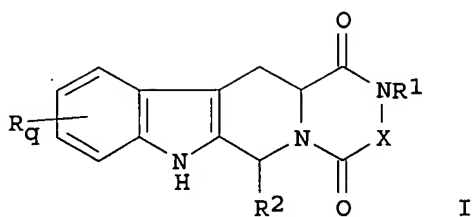
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010166	A1	20020207	WO 2001-US21678	20010709
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1305313	A1	20030502	EP 2001-951008	20010709
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRIORITY APPLN. INFO.:			US 2000-222451P	P 20000802
			WO 2001-US21678	W 20010709
OTHER SOURCE(S):	MARPAT 136:151441			
GI				



AB Compds. I [$R' = \text{halo, alkyl}; q = 0-4; R_1 = \text{H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, cycloalkylalkyl, arylalkyl, heteroarylalkyl}; R_2$ is an optionally substituted monocyclic arom. ring selected from benzene, thiophene, furan, and pyridine or an optionally substituted bicyclic ring; $X = \text{NH or substituted imino, O, S, substituted methylene or ethylene};$ the substituents may form addnl. rings] and their salts and solvates were prepd. for use as phosphodiesterase (PDE) inhibitors. Thus, compd. II was prepd. by a multistep procedure starting with coupling of L-tryptophan Me ester with CbzNMeCMe₂CO₂H (Cbz = benzyloxycarbonyl) and showed IC₅₀ = 161.0 nM for inhibition of cGMP-PDE.

IT 395665-59-5P 395665-72-2P

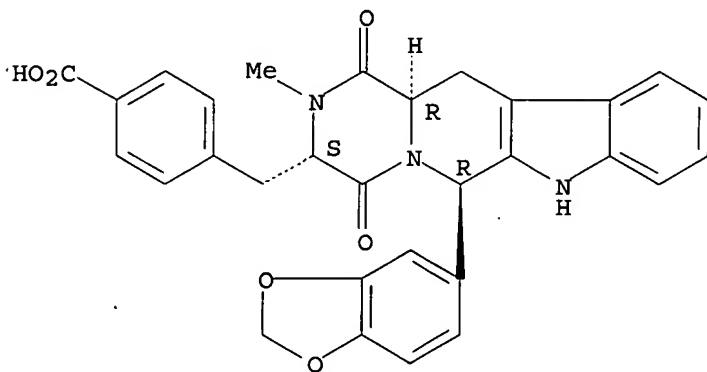
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of fused heterocyclic derivs. as phosphodiesterase inhibitors)

RN 395665-59-5 CAPLUS

CN Benzoic acid, 4-[[[(3S,6R,12aR)-6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

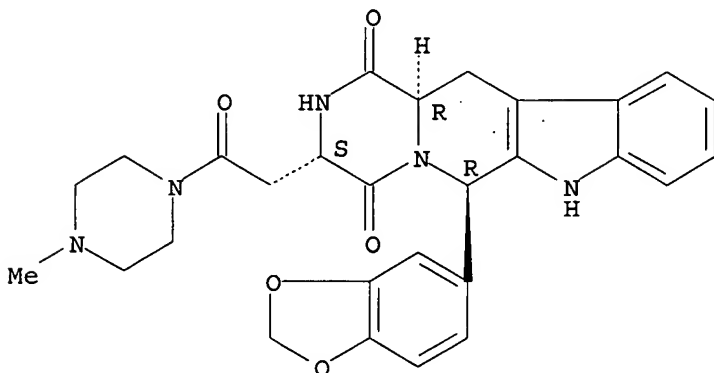


10/ 068,114

RN 395665-72-2 CAPLUS

CN Piperazine, 1-[[[(3S,6R,12aR)-6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]acetyl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:10475 CAPLUS

DOCUMENT NUMBER: 136:85828

TITLE: Preparation of pyrazinopyridoindolediones as cyclic GMP phosphodiesterase inhibitors

INVENTOR(S): Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.; Daugan, Alain Claude-Marie; Gellibert, Françoise

PATENT ASSIGNEE(S): Lilly Icos LLC, USA

SOURCE: PCT Int. Appl., 81 pp.

CODEN: PIXXD2

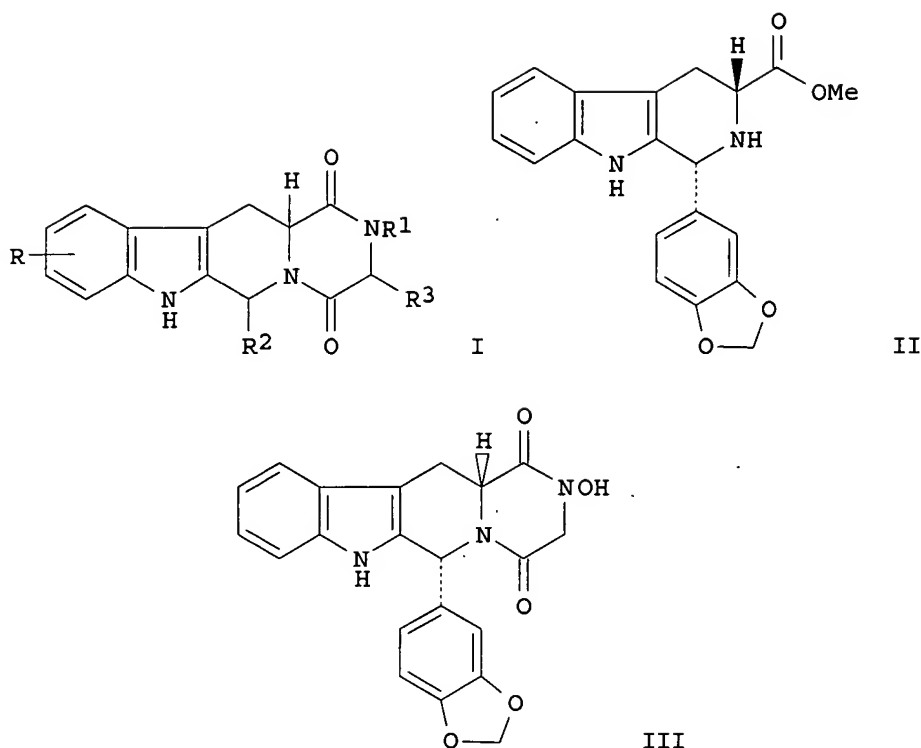
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000656	A2	20020103	WO 2001-US15935	20010515
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001061707	A5	20020108	AU 2001-61707	20010515
PRIORITY APPLN. INFO.:			US 2000-213647P	P 20000623
			WO 2001-US15935	W 20010515
OTHER SOURCE(S):		MARPAT 136:85828		
GI				



AB The pyrazinopyridoindolediones I (R = halo, C1-6-alkyl; R1 = aryl, heteroaryl, amino, R4O, R4CO, R4SO, R4SO₂, C1-4-alkylene-CO₂R₄, C1-4-alkyleneheteroaryl, sulfamoyl, cyano, NO₂, CO-C1-4-alkyleneheteroaryl, C1-4-alkylene-OR₄, etc.; R2 = monocyclic arom. ring consisting of benzene, thiophene, furan, and pyridine, and an optionally substituted bicyclic ring wherein the fused ring is a 5- or 6-membered ring comprised of C and optionally heteroatoms selected from O, S, and N; R3 = H, C1-6-alkyl; R4 = H, alkyl, aryl, heteroaryl, etc.) and their salts and solvates were prepd. as cyclic GMP phosphodiesterase inhibitors. Thus, D-tryptophan Me ester hydrochloride was treated with piperonal to give the carbolinecarboxylate II, which was treated with chloroacetyl chloride followed by cyclization with hydroxylamine-HCl to give the pyrazinopyridoindoledione III. The cyclic GMP phosphodiesterase inhibitor IC₅₀ of III 0.0075 .mu.M.

IT 385769-78-8P 385770-20-7P 385770-29-6P
385770-46-7P 385770-54-7P 385770-68-3P
385770-70-7P 385770-72-9P 385770-75-2P
385770-93-4P

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

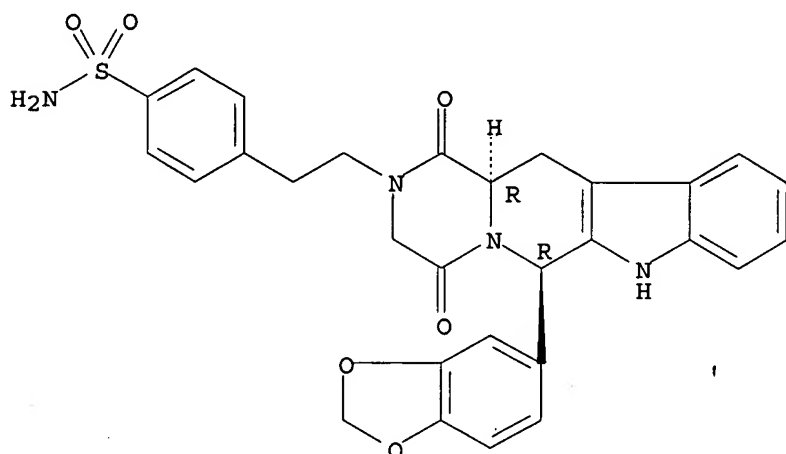
(prepn. of pyrazinopyridoindolediones as cyclic GMP phosphodiesterase inhibitors)

RN 385769-78-8 CAPLUS

CN Benzenesulfonamide, 4-[2-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

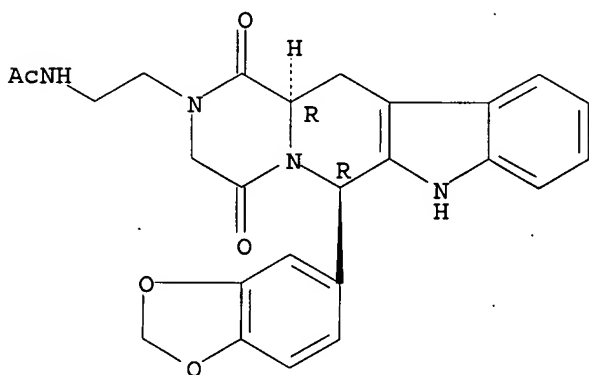
10/ 068,114



RN 385770-20-7 CAPLUS

CN Acetamide, N-[2-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]ethyl]-(9CI) (CA INDEX NAME)

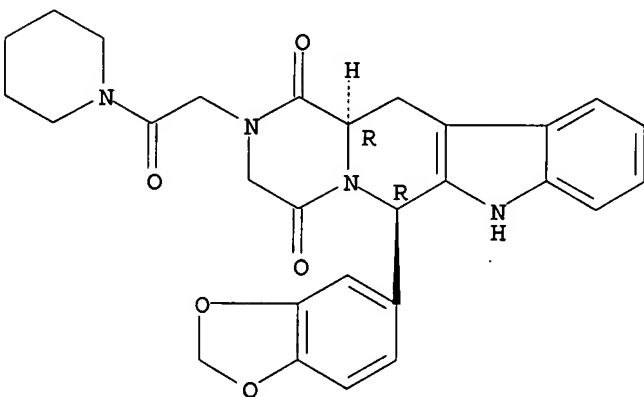
Absolute stereochemistry.



RN 385770-29-6 CAPLUS

CN Piperidine, 1-[[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

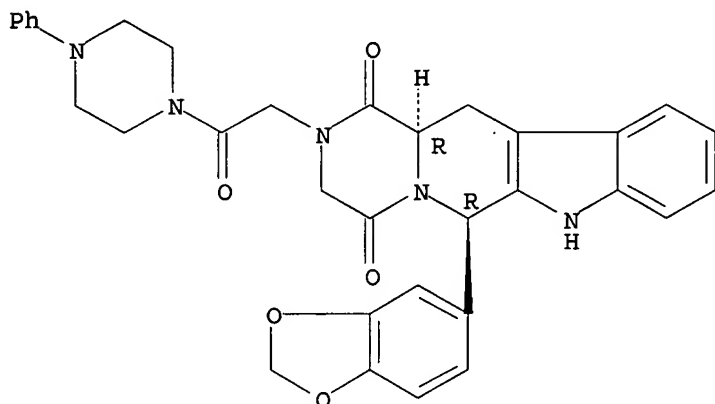


10/ 068,114

RN 385770-46-7 CAPLUS

CN Piperazine, 1-[[(6R,12aR) -6- (1,3-benzodioxol-5-yl) -3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

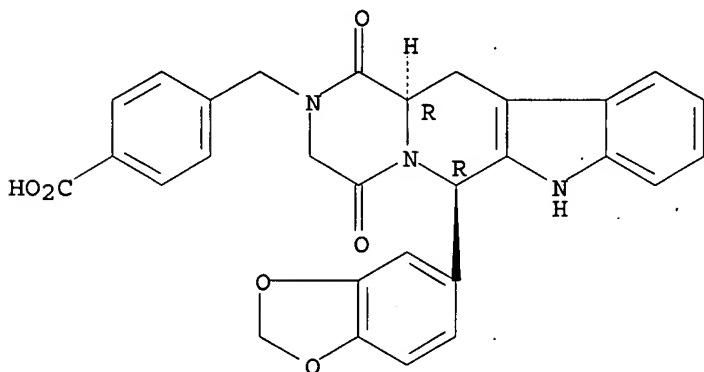
Absolute stereochemistry.



RN 385770-54-7 CAPLUS

CN Benzoic acid, 4-[[(6R,12aR) -6- (1,3-benzodioxol-5-yl) -3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

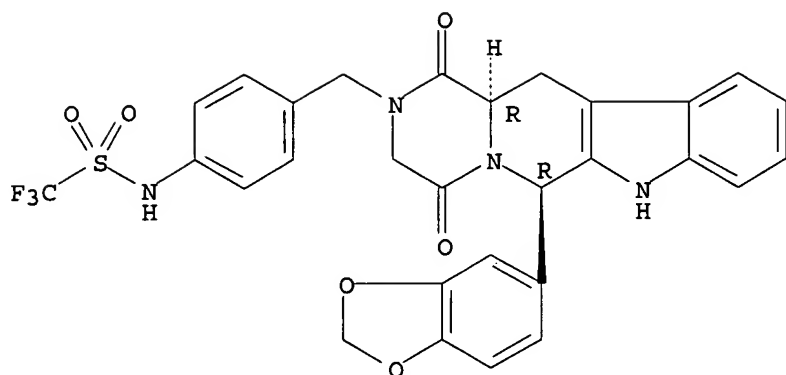
Absolute stereochemistry.



RN 385770-68-3 CAPLUS

CN Methanesulfonamide, N-[4-[[(6R,12aR) -6- (1,3-benzodioxol-5-yl) -3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]phenyl]-1,1,1-trifluoro- (9CI) (CA INDEX NAME)

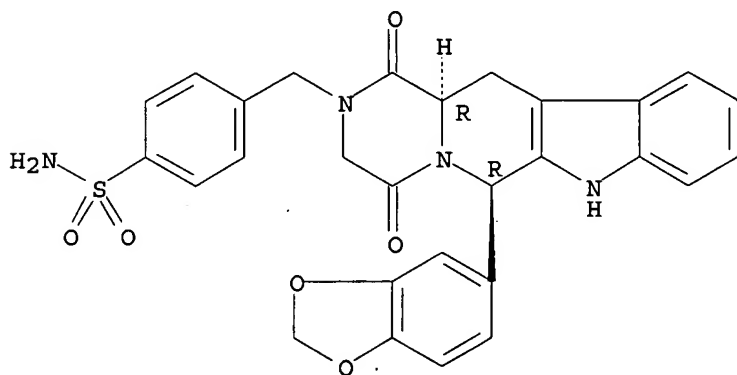
Absolute stereochemistry.



RN 385770-70-7 CAPLUS

CN Benzenesulfonamide, 4-[[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]-(9CI) (CA INDEX NAME)

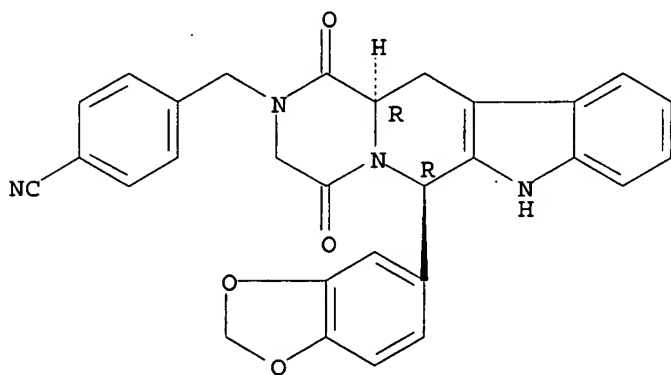
Absolute stereochemistry.



RN 385770-72-9 CAPLUS

CN Benzonitrile, 4-[[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



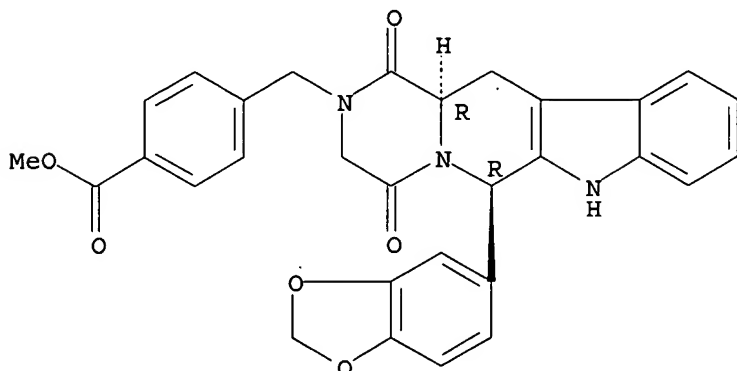
RN 385770-75-2 CAPLUS

CN Benzoic acid, 4-[[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]-(9CI) (CA INDEX NAME)

10/ 068,114

, methyl ester (9CI) (CA INDEX NAME)

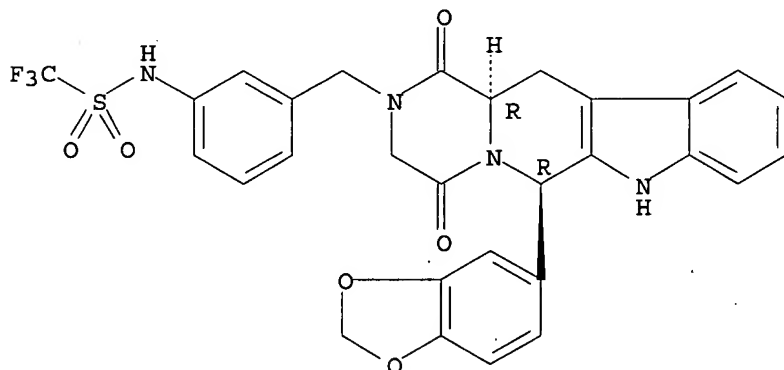
Absolute stereochemistry.



RN 385770-93-4 CAPLUS

CN Methanesulfonamide, N-[3-[[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]phenyl]-1,1,1-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:904178 CAPLUS

DOCUMENT NUMBER: 136:37622

TITLE: Synthesis of caboxamidoquinazolines as caspase inhibitors

INVENTOR(S): Charrier, Jean-Damien; Brenchley, Guy

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094351	A1	20011213	WO 2001-US18243	20010605
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,				

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1289993 A1 20030312 EP 2001-941972 20010605

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

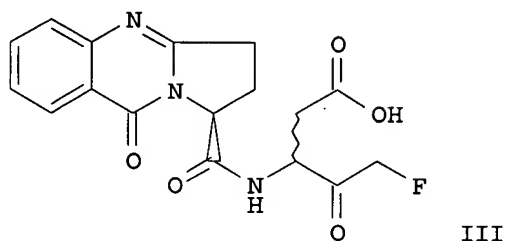
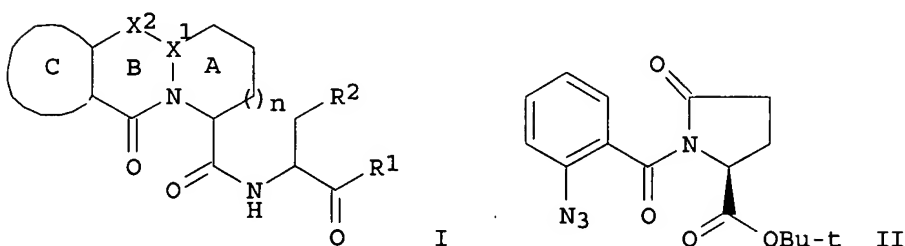
US 2002045623 A1 20020418 US 2001-877832 20010607

PRIORITY APPLN. INFO.: US 2000-209929P P 20000607

WO 2001-US18243 W 20010605

OTHER SOURCE(S): MARPAT 136:37622

GI



AB Title compds. I [R1 is H, CHN2, R, CH2Y; R is an aliph. group, an aryl group, an aralkyl group, a heterocyclic group, or a heterocyclalkyl group; Y is an electroneg. leaving group; R2 is CO2H, CH2CO2H, or esters, amides or isosteres thereof; X2-X1 is NR3-CR3, C(R3)2-CR3, C(R3)2-N, N:C, CR3:N, C(R3):C, C(O)-N, or C(O)-C(R3); R3 is selected from hydrogen alkyl; Ring C is a fused aryl ring; n is 0 - 2; and each methylene carbon in Ring A is (un)substituted by :O or by one or more halo, alkyl or alkoxy] were prepd. Six synthetic examples were provided. E.g., (S)-5-oxoproline tert-Bu ester was acylated with 2-azidobenzoyl chloride (THF, LDA, -78.degree.C, 1 h) to give intermediate II. Azide II was treated with Ph3P (xylene, room temp.) which resulted in cyclization to the tricyclic intermediate. This intermediate was deprotected (TFA, room temp.) and the resulting carboxylic acid coupled to 3-amino-5-fluoro-4-hydroxypenatanoic acid tert-Bu ester (THF, EDC, HOBT, DMAP, room temp., 18 h) and the resulting alc. oxidized (CH2Cl2, Dess-Martin periodinane, room temp., 18 h) and finally deprotected to give (CH2Cl2, TFA, room temp., 30 min) to give III in 34% overall yield. III had Ki = 160,500 M-1s-1 for caspase-3. Example compds. also inhibited IL-1.beta. secretion and showed activity in the FAS induced apoptosis assay. I are useful for treating caspase-mediated diseases.

10/ 068,114

IT 380223-06-3P

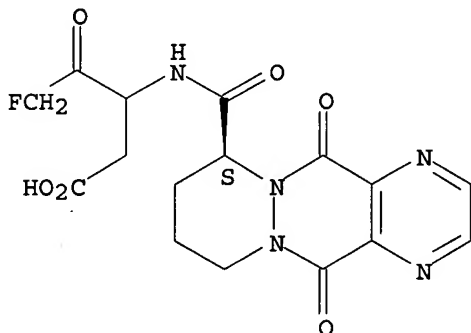
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; synthesis of caboxamidoquinazolines as caspase inhibitors)

RN 380223-06-3 CAPLUS

CN Pentanoic acid, 5-fluoro-3-[[[(7S)-5,7,8,9,10,12-hexahydro-5,12-dioxopyrazino[2,3-d]pyridazino[1,2-a]pyridazin-7-yl]carbonyl]amino]-4-oxo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:904172 CAPLUS

DOCUMENT NUMBER: 136:20091

TITLE: Preparation of tetracyclic diketopiperazine compounds as PDE5 inhibitor

INVENTOR(S): Orme, Mark W.; Daugan, Alain Claude-Marie; Bombrun, Agnes

PATENT ASSIGNEE(S): Lilly Icos Llc, USA

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

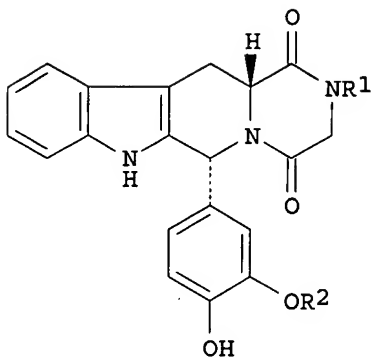
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094347	A1	20011213	WO 2001-US15937	20010515
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1289990	A1	20030312	EP 2001-945961	20010515
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 2003153575	A1	20030814	US 2002-296099	20021122
PRIORITY APPLN. INFO.:			US 2000-210324P P	20000608
			WO 2001-US15937 W	20010515
OTHER SOURCE(S):	MARPAT 136:20091			

GI



AB The title compds. I [R1 = C1-6 alkyl; R2 = H, Me] were prepd. and use of the compds. as PDE5 inhibitors was described.. E.g., (6R,12aR)-6-(3,4-dihydroxyphenyl)-2-methyl-2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione was prepd. I may be used for male erectile dysfunction or female arousal disorder.

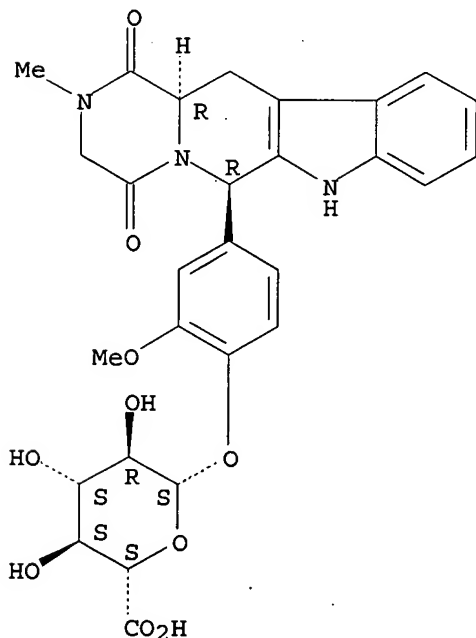
IT 378788-18-2P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. of tetracyclic diketopiperazine compds. as PDE5 inhibitor)

RN 378788-18-2 CAPLUS

CN .beta.-D-Glucopyranosiduronic acid, 2-methoxy-4-[(6R,12aR)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxypyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:177398 CAPLUS

DOCUMENT NUMBER: 135:29005

TITLE: Evidence for Gliotoxin-Glutathione conjugate adducts

AUTHOR(S): Bernardo, P. H.; Chai, C. L. L.; Deeble, G. J.; Liu, X.-M.; Waring, P.

CORPORATE SOURCE: Department of Chemistry, Faculties, Australian National University, 0200, Australia

SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(4), 483-485

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The equil. const. for the gliotoxin/glutathione pair was found to be $1200 \pm 100 \text{ M}^{-1}$ at pH 7.0 at 25 .degree.C. Under conditions where the reaction was quenched rapidly with the addn. of acid, gliotoxin-glutathione conjugate adducts were detected.

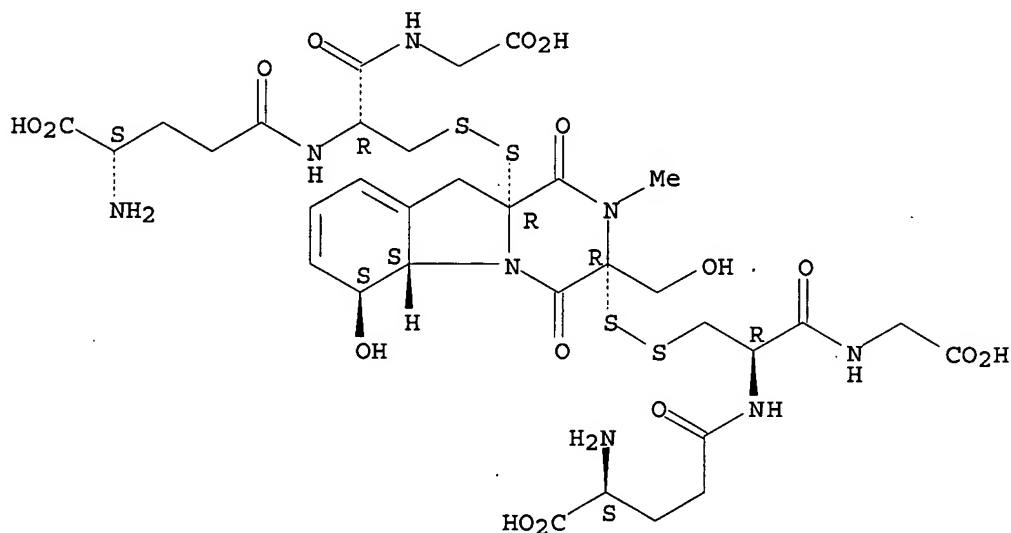
IT 343946-99-6 343947-01-3 343947-03-5

RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)
(evidence for gliotoxin-glutathione conjugate adducts formation)

RN 343946-99-6 CAPLUS

CN Glycine, 23,2'3-[[[(3R,5aS,6S,10aR)-1,2,3,4,6,10-hexahydro-6-hydroxy-3-(hydroxymethyl)-2-methyl-1,4-dioxopyrazino[1,2-a]indole-3,10a(5aH)-diyl]bis(dithio)]bis[L-.gamma.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

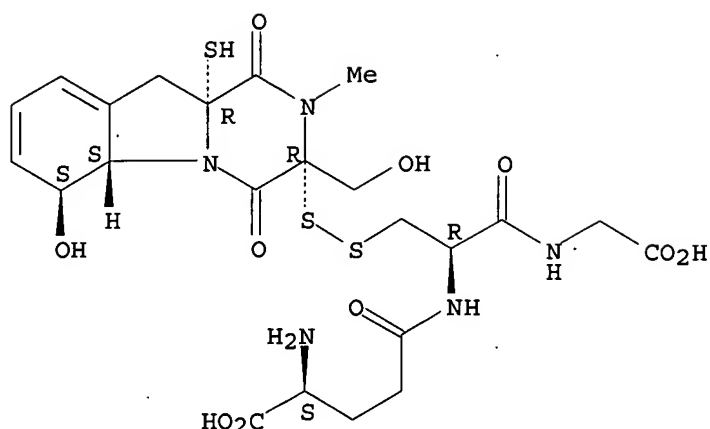
Absolute stereochemistry.



RN 343947-01-3 CAPLUS

CN Glycine, L-.gamma.-glutamyl-3-[[[(3R,5aS,6S,10aR)-1,2,3,4,5a,6,10,10a-octahydro-6-hydroxy-3-(hydroxymethyl)-10a-mercapto-2-methyl-1,4-dioxopyrazino[1,2-a]indol-3-yl]dithio]-L-alanyl- (9CI) (CA INDEX NAME)

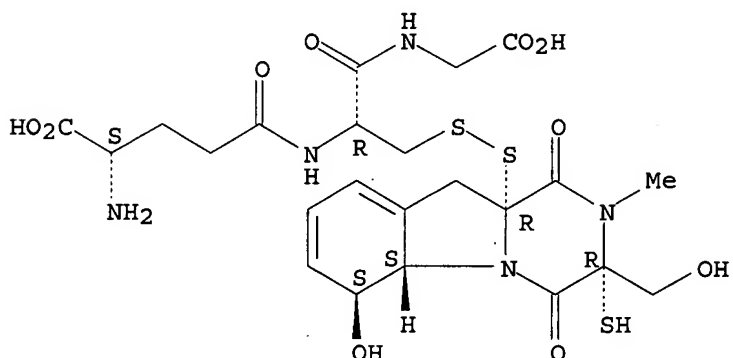
Absolute stereochemistry.



RN 343947-03-5 CAPLUS

CN Glycine, L-.gamma.-glutamyl-3-[[(3R,5aS,6S,10aR)-1,2,3,4,6,10-hexahydro-6-hydroxy-3-(hydroxymethyl)-3-mercapto-2-methyl-1,4-dioxopyrazino[1,2-a]indol-10a(5aH)-yl]dithio]-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:872654 CAPLUS

DOCUMENT NUMBER: 134:216800

TITLE: Inhibition of BCRP-mediated drug efflux by fumitremorgin-type indolyl diketopiperazines

AUTHOR(S): van Loevezijn, A.; Allen, J. D.; Schinkel, A. H.; Koomen, G.-J.

CORPORATE SOURCE: Institute of Molecular Chemistry, Laboratory of Organic Chemistry, University of Amsterdam, Amsterdam, NL-1018 WS, Neth.

SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), Volume Date 2001, 11(1), 29-32
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A library of 42 diastereoisomeric mixts. of fumitremorgin-type indolyl diketopiperazines, prepd. by parallel solid-phase synthesis, was screened for breast cancer resistance protein inhibitory activity and compared with GF120918. Demethoxy-fumitremorgin C was synthesized (no data) by

solid-phase techniques and tested as well. Structure-activity relationship studies have identified several potent analogs, both in assays using the T6400 mouse and the T8 human cell line, whereas low cytotoxicity was seen at effective concns.

IT 211359-66-9 211359-68-1 211359-70-5

211359-71-6 329356-40-3 329356-41-4

329356-42-5

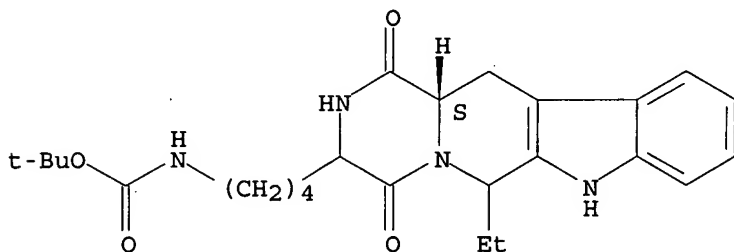
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(inhibition of breast cancer-resistance protein-mediated drug efflux by fumitremorgin-type indolyl diketopiperazines)

RN 211359-66-9 CAPLUS

CN Carbamic acid, [4-[(12aS)-6-ethyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

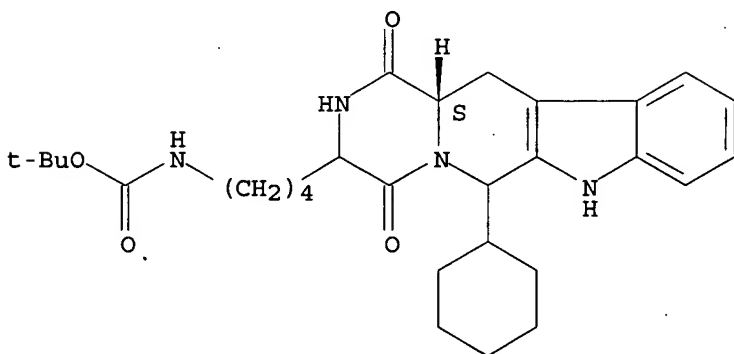
Absolute stereochemistry.



RN 211359-68-1 CAPLUS

CN Carbamic acid, [4-[(12aS)-6-cyclohexyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

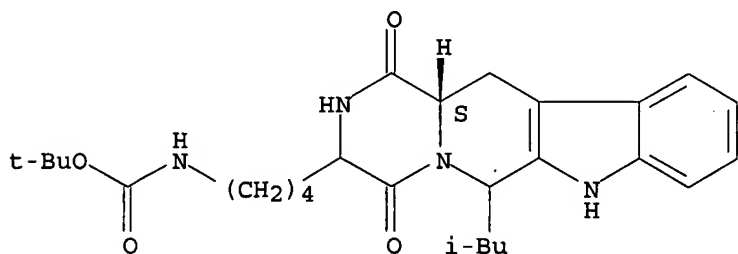
Absolute stereochemistry.



RN 211359-70-5 CAPLUS

CN Carbamic acid, [4-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

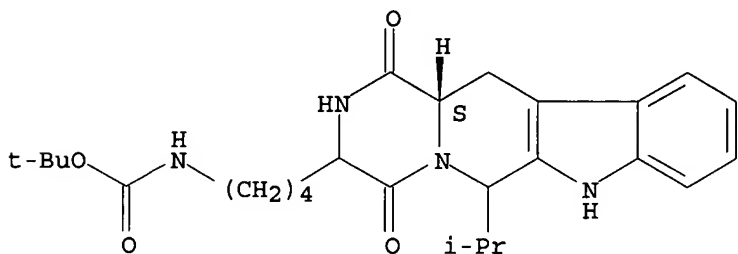
Absolute stereochemistry.



RN 211359-71-6 CAPLUS

CN Carbamic acid, [4-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(1-methylethyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

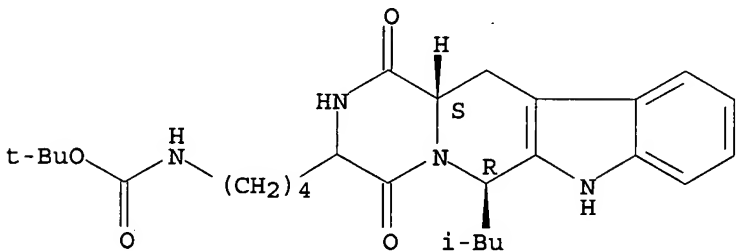
Absolute stereochemistry.



RN 329356-40-3 CAPLUS

CN Carbamic acid, [4-[(6R,12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

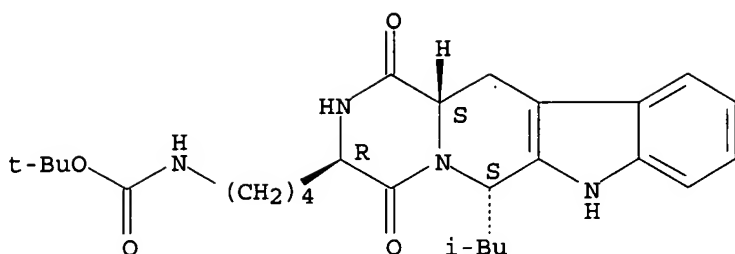
Absolute stereochemistry.



RN 329356-41-4 CAPLUS

CN Carbamic acid, [4-[(3R,6S,12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

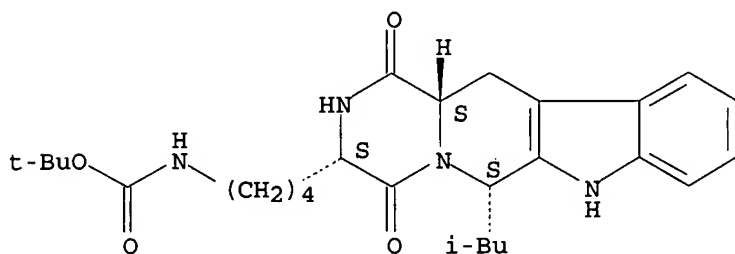
Absolute stereochemistry.



RN 329356-42-5 CAPLUS

CN Carbamic acid, [4-[(3S,6S,12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:785898 CAPLUS

DOCUMENT NUMBER: 133:329627

TITLE: Tetracyclic cGMP-specific phosphodiesterase inhibitors and their use in disease treatment

INVENTOR(S): Daugan, Alain Claude Marie; Gellibert, Françoise

PATENT ASSIGNEE(S): Icos Corp., USA

SOURCE: U.S., 30 pp., Cont.-in-part of PCT 9519978.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

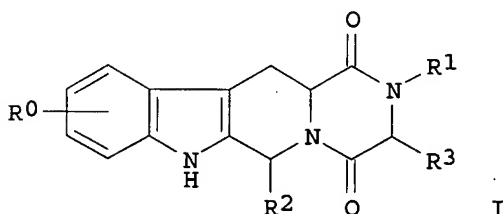
FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6143746	A	20001107	US 1998-154051	19980916
WO 9519978	A1	19950727	WO 1995-EP183	19950119
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
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WO 9703675	A1	19970206	WO 1996-EP3024	19960711
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 WO 9703985 A1 19970206 WO 1996-EP3025 19960711
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 US 6025494 A 20000215 US 1998-133078 19980812
 CA 2340636 AA 20000323 CA 1999-2340636 19990826
 EP 1113800 A1 20010711 EP 1999-945201 19990826
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 JP 2002524516 T2 20020806 JP 2000-569812 19990826
 US 6127542 A 20001003 US 1999-399667 19990921
 US 6369059 B1 20020409 US 2000-633431 20000807
 CZ 289832 B6 20020417 CZ 2000-3428 20000919
 US 2002119976 A1 20020829 US 2002-68114 20020205
 PRIORITY APPLN. INFO.: GB 1994-1090 A 19940121
 WO 1995-EP183 A2 19950119
 GB 1995-14464 A 19950714
 GB 1995-14465 A 19950714
 WO 1996-EP3024 A2 19960711
 WO 1996-EP3025 A2 19960711
 CZ 1998-33 A3 19960711
 US 1996-669389 A3 19960716
 US 1998-133078 A1 19980812
 US 1998-154051 A 19980916
 WO 1999-US19466 W 19990826
 US 1999-399667 A1 19990921
 US 2000-633431 A1 20000807

OTHER SOURCE(S): MARPAT 133:329627
 GI



AB A compd. of formula I (R0 = H, halogen, C1-6 alkyl; R1 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, halo-C1-6 alkyl, C3-8 cycloalkyl, C3-8 cycloalkyl-C1-3 alkyl, aryl-C1-3 alkyl, heteroaryl-C1-3 alkyl; R2 = (substituted) monocyclic arom. ring selected from benzene, thiophene, furan, and pyridine, or (substituted) bicyclic ring (a) attached to the rest of the mol. via one of the benzene ring carbon atoms, and wherein the fused ring is a 5- or 6-membered ring which may be satd. or partially or fully unsatd., and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulfur, and nitrogen; R3 = H, C1-3 alkyl, or R1 and R3 together = 3- or 4-membered alkyl or alkenyl chain) and salts and solvates thereof is disclosed. Compd. I is a potent and selective inhibitor of cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase, having a utility in a variety of therapeutic areas where such inhibition is beneficial, including the treatment of cardiovascular disorders and erectile dysfunction. Thus, many I compds. were synthesized and tested in vitro as inhibitors of cGMP

10/ 068,114

phosphodiesterase. Cis-2,3,6,7,12,12a-hexahydro-2-(4-pyridylmethyl)-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione showed IC50 of 10 nM.

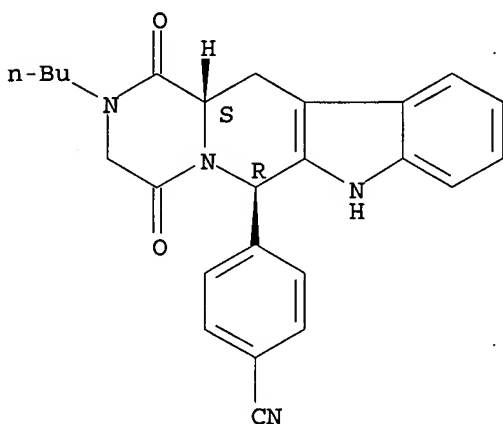
IT 171488-69-0P 171488-89-4P 171488-90-7P
303984-33-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tetracyclic cyclic GMP-specific phosphodiesterase inhibitors and their use in disease treatment)

RN 171488-69-0 CAPLUS

CN Benzonitrile, 4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-, rel- (9CI) (CA INDEX NAME)

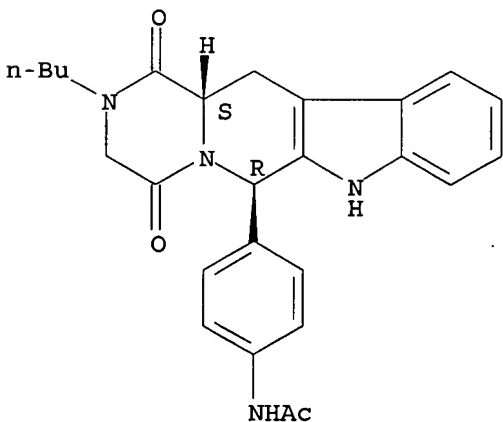
Relative stereochemistry.



RN 171488-89-4 CAPLUS

CN Acetamide, N-[4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

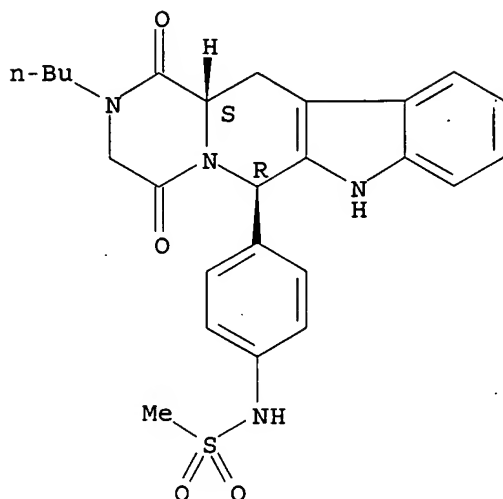


RN 171488-90-7 CAPLUS

CN Methanesulfonamide, N-[4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

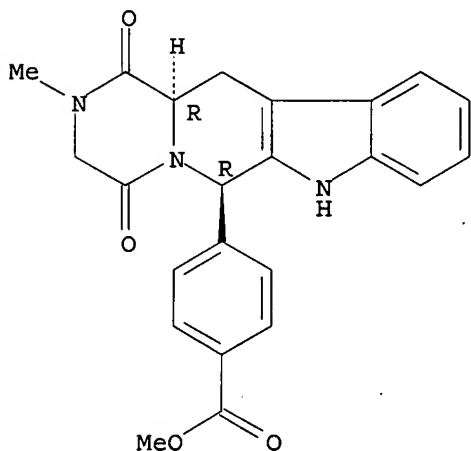
10/ 068,114

Relative stereochemistry.



RN 303984-33-0 CAPLUS
CN Benzoic acid, 4-[(6R,12aR)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:758774 CAPLUS
DOCUMENT NUMBER: 134:56943
TITLE: N-Terminal Peptide Aldehydes as Electrophiles in Combinatorial Solid Phase Synthesis of Novel Peptide Isosteres
AUTHOR(S): Groth, Thomas; Meldal, Morten
CORPORATE SOURCE: Center for Solid Phase Organic Combinatorial Chemistry, Department of Chemistry, Carlsberg Laboratory, Valby, DK-2500, Den.
SOURCE: Journal of Combinatorial Chemistry (2001), 3(1), 45-63
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 134:56943

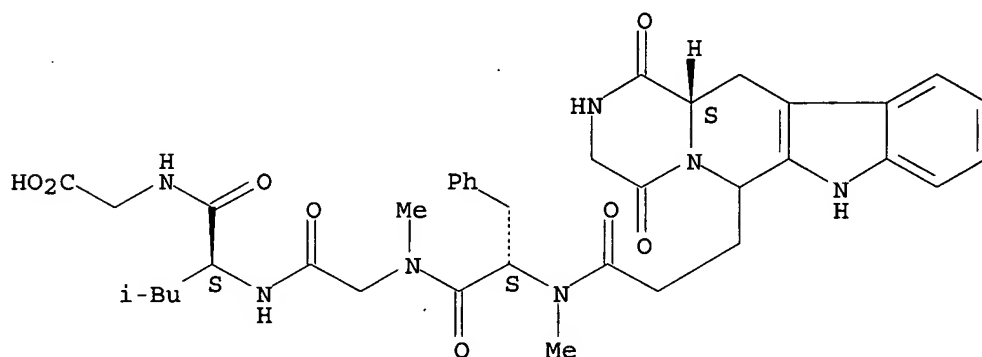
AB N-Terminal peptide aldehydes were synthesized on a solid support and utilized as electrophiles in nucleophilic reactions in order to furnish novel and diverse peptide isosteres. The aldehyde moiety of the peptide was synthesized by coupling a protected aldehyde building block to the peptide and deprotecting it quant. in less than 3 min. It was found that protection of the two succeeding amide nitrogens was necessary in order to avoid reaction between the aldehyde and backbone amides. The N-terminal peptide aldehydes were successfully reacted in the following way: (a) reductive amination with a large variety of amines, leading to N-alkyl-.gamma.-aminobutyric peptide isosteres positioned centrally in the peptide; (b) reductive amination with amino esters, leading to N-terminal 2,5-diketopiperazine peptides; (c) Horner-Wadsworth-Emmons olefination, leading to unsatd. peptide isosteres positioned centrally in the peptide; and (d) Pictet-Spengler condensations, leading to tetrahydro-.beta.-carboline either positioned centrally in a peptide or fused with a diketopiperazine ring in the N-terminus of the peptide.

IT 313695-12-4DP, resin-bound 313695-13-5DP, resin-bound
 313695-14-6DP, resin-bound
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (terminal peptide aldehydes as electrophiles in combinatorial solid phase synthesis of novel peptide isosteres)

RN 313695-12-4 CAPLUS

CN Glycine, N-methyl-N-[3-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-1-oxopropyl]-L-phenylalanyl-N-methylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

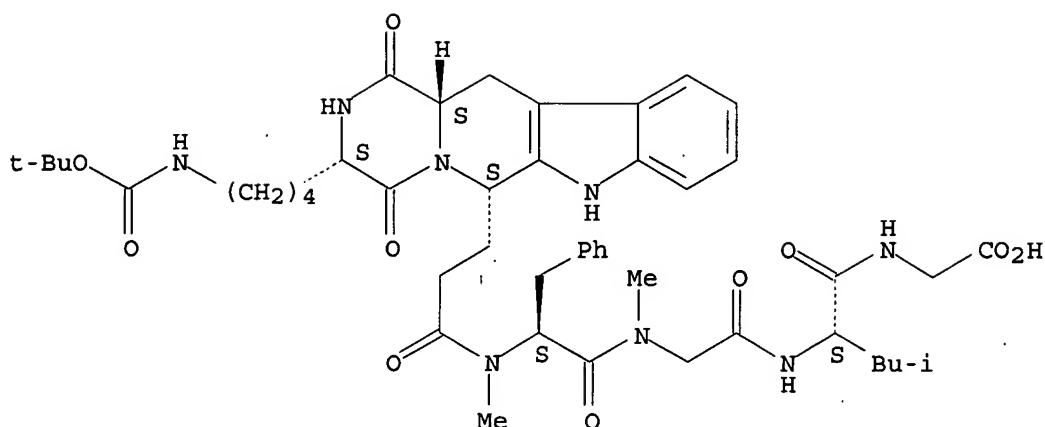
Absolute stereochemistry.



RN 313695-13-5 CAPLUS

CN Glycine, N-[3-[(3S,6S,12aS)-3-[4-[[1,1-dimethylethoxy]carbonyl]amino]butyl]-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-1-oxopropyl]-N-methyl-L-phenylalanyl-N-methylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

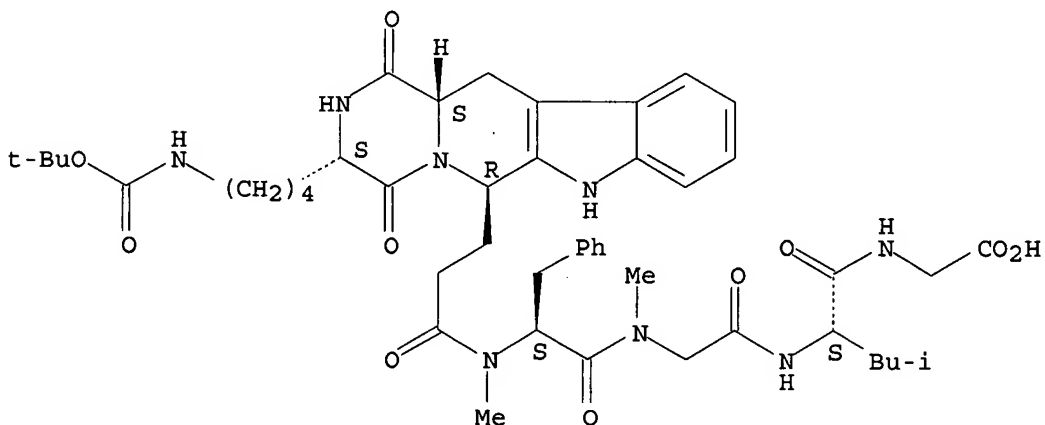
Absolute stereochemistry.



RN 313695-14-6 CAPLUS

CN Glycine, N-[3-[(3S,6R,12aS)-3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]butyl]-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-1-oxopropyl]-N-methyl-L-phenylalanyl-N-methylglycyl-L-leucyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:487536 CAPLUS

DOCUMENT NUMBER: 131:129985

TITLE: Oxazolidines substituted by tricyclic indoles

INVENTOR(S): Ruppelt, Martin; Bartel, Stephan; Guarnieri, Walter; Raddatz, Siegfried; Rosentreter, Ulrich; Wild, Hanno; Endermann, Rainer; Kroll, Hein-Peter

PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: Ger. Offen., 40 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

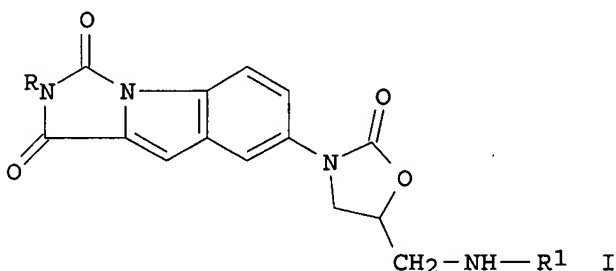
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

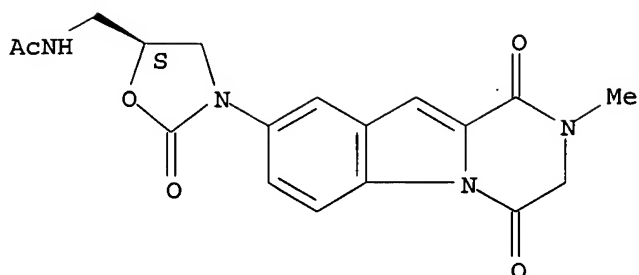
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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DE 19802235 A1 19990729 DE 1998-19802235 19980122
 WO 9937652 A1 19990729 WO 1999-EP97 19990109
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
 DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
 KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
 MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
 TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
 TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 9924206 A1 19990809 AU 1999-24206 19990109
 EP 1049701 A1 20001108 EP 1999-903616 19990109
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 JP 2002501073 T2 20020115 JP 2000-528573 19990109
 PRIORITY APPLN. INFO.: DE 1998-19802235 A 19980122
 WO 1999-EP97 W 19990109
 OTHER SOURCE(S): MARPAT 131:129985
 GI



- AB Approx. 25 antibacterial title compds. such as I (R = benzyl, p-methoxybenzyl, allyl, Bu, cyclohexyl, Et, Me; R¹ = Ac, EtCO, CO₂Me) were prepd. E.g., N-[3-(2-(ethoxycarbonyl)-5-indolylamino)-2-hydroxypropyl]acetamide was cyclized with carbonyldiimidazole to give 85% 3-(2-ethoxycarbonyl-5-indolyl)-5-(acetaminomethyl)-2-oxazolidinone. The MIC of I (R = Bu, R¹ = Ac) was 4 .mu.g/mL against Staphylococcus Aureus.
- IT 234770-40-2P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (prepn. and bactericidal activity of oxazolidines substituted by tricyclic indoles)
- RN 234770-40-2 CAPLUS
- CN Acetamide, N-[[[(5S)-2-oxo-3-(1,2,3,4-tetrahydro-2-methyl-1,4-dioxypyrazino[1,2-a]indol-8-yl)-5-oxazolidinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



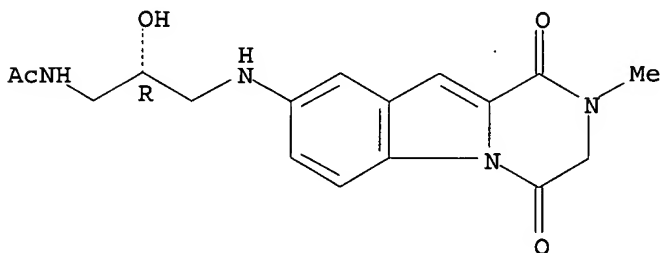
IT 234770-54-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and bactericidal activity of oxazolidines substituted by
tricyclic indoles)

RN 234770-54-8 CAPLUS

CN Acetamide, N-[(2R)-2-hydroxy-3-[(1,2,3,4-tetrahydro-2-methyl-1,4-
dioxypyrazino[1,2-a]indol-8-yl)amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:396840 CAPLUS

DOCUMENT NUMBER: 129:175833

TITLE: Solid-phase synthesis of fumitremorgin, verruculogen
and tryprostatin analogs based on a
cyclization/cleavage strategy

AUTHOR(S): Van Loevezijn, Arnold; Van Maarseveen, Jan H.;
Stegman, Karel; Visser, Geb M.; Koomen, Gerrit-Jan

CORPORATE SOURCE: Laboratory of Organic Chemistry, Institute of
Molecular Chemistry, University of Amsterdam,
Amsterdam, NL-1018 WS, Neth.

SOURCE: Tetrahedron Letters (1998), 39(26), 4737-4740
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A solid phase synthesis towards structural analogs of fumitremorgins,
verruculogens and tryprostatins using a cyclization/cleavage strategy was
developed. To prove the general applicability of the route, a
representative set of 42 single compds. (as diastereomeric mixts.) was
prepd. by parallel synthesis and analyzed with LC/MS.

IT 211359-66-9P 211359-68-1P 211359-70-5P
211359-71-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of fumitremorgin, verruculogen and tryprostatin
analog based on a cyclization/cleavage strategy)

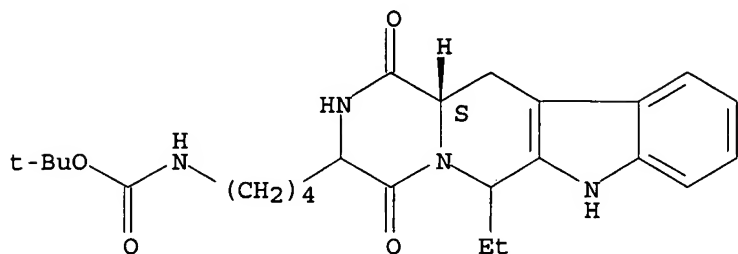
RN 211359-66-9 CAPLUS

CN Carbamic acid, [4-[(12aS)-6-ethyl-1,2,3,4,6,7,12,12a-octahydro-1,4-

10/ 068,114

dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

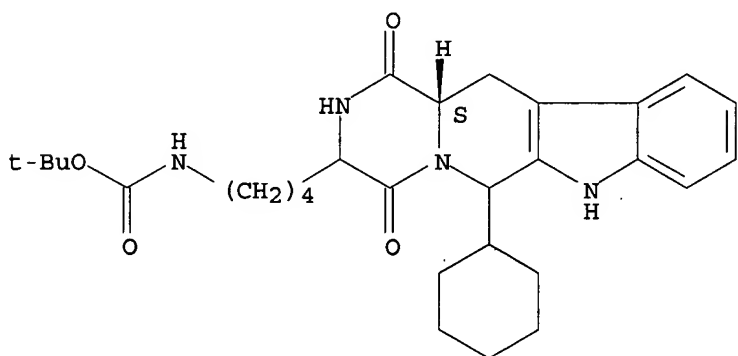
Absolute stereochemistry.



RN 211359-68-1 CAPLUS

CN Carbamic acid, [4-[(12aS)-6-cyclohexyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

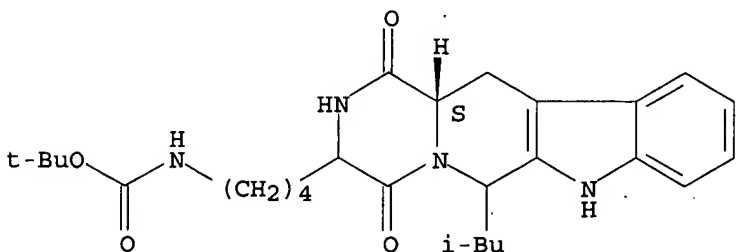
Absolute stereochemistry.



RN 211359-70-5 CAPLUS

CN Carbamic acid, [4-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(1-methylethyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

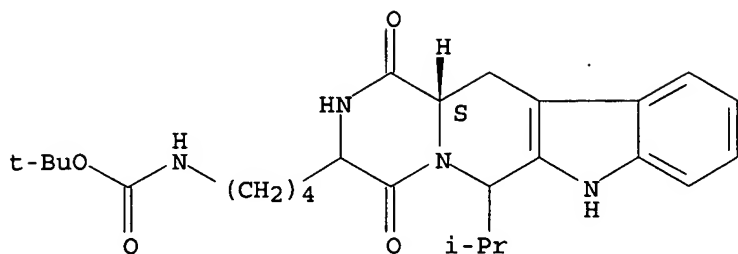
Absolute stereochemistry.



RN 211359-71-6 CAPLUS

CN Carbamic acid, [4-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(1-methylethyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:986316 CAPLUS

DOCUMENT NUMBER: 124:55977

TITLE: Preparation of pyrazinopyridoindole derivatives as inhibitors of cyclic guanosine 3',5'-monophosphate specific phosphodiesterase

INVENTOR(S): Daugan, Alain Claude-Marie

PATENT ASSIGNEE(S): Laboratoires Glaxo S.A., Fr.

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9519978	A1	19950727	WO 1995-EP183	19950119
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
HR 950023	B1	20001031	HR 1995-950023	19950117
TW 378210	B	20000101	TW 1995-84100415	19950118
CA 2181377	AA	19950727	CA 1995-2181377	19950119
CA 2181377	C	20020528		
AU 9515748	A1	19950808	AU 1995-15748	19950119
AU 689205	B2	19980326		
ZA 9500424	A	19950927	ZA 1995-424	19950119
EP 740668	A1	19961106	EP 1995-907565	19950119
EP 740668	B1	19980729		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1143963	A	19970226	CN 1995-192078	19950119
CN 1045777	B	19991020		
HU 74943	A2	19970328	HU 1996-1982	19950119
JP 09508113	T2	19970819	JP 1995-519339	19950119
BR 9506559	A	19971028	BR 1995-6559	19950119
AT 169018	E	19980815	AT 1995-907565	19950119
IL 112384	A1	19980816	IL 1995-112384	19950119
ES 2122543	T3	19981216	ES 1995-907565	19950119
RU 2142463	C1	19991210	RU 1996-117127	19950119
CZ 286566	B6	20000517	CZ 1996-2116	19950119
SK 280879	B6	20000814	SK 1996-940	19950119
PL 179744	B1	20001031	PL 1995-315559	19950119
RO 117794	B1	20020730	RO 1996-1454	19950119
LV 11690	B	19970620	LV 1996-228	19960710

10/ 068,114

US 5859006	A	19990112	US 1996-669389	19960716
FI 9602927	A	19960719	FI 1996-2927	19960719
NO 9603015	A	19960909	NO 1996-3015	19960719
AU 9873912	A1	19980820	AU 1998-73912	19980626
AU 707055	B2	19990701		
US 6025494	A	20000215	US 1998-133078	19980812
US 6143746	A	20001107	US 1998-154051	19980916
CN 1224720	A	19990804	CN 1998-122779	19981201
CN 1070492	B	20010905		
HK 1013286	A1	20000519	HK 1998-114572	19981222
US 6127542	A	20001003	US 1999-399667	19990921
US 6369059	B1	20020409	US 2000-633431	20000807
US 2002119976	A1	20020829	US 2002-68114	20020205

PRIORITY APPLN. INFO.:

GB 1994-1090	A	19940121
WO 1995-EP183	W	19950119
GB 1995-14464	A	19950714
GB 1995-14465	A	19950714
WO 1996-EP3024	A2	19960711
WO 1996-EP3025	A2	19960711
US 1996-669389	A3	19960716
US 1998-133078	A1	19980812
US 1999-399667	A1	19990921
US 2000-633431	A1	20000807

OTHER SOURCE(S): MARPAT 124:55977

GI For diagram(s), see printed CA Issue.

AB The title compds. I [R represents hydrogen, halogen or C1-6 alkyl; R1 represents hydrogen, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, haloC1-6alkyl, C3-8cycloalkyl, etc.; R2 represents an optionally substituted monocyclic arom. ring selected from benzene, thiophene, furan and pyridine or an optionally substituted bicyclic ring Q1 attached to the rest of the mol. via one of the benzene ring carbon atoms and wherein the fused ring A is a 5- or 6-membered ring which may be satd. or partially or fully unsatd. and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulfur and nitrogen; and R3 represents hydrogen or C1-3 alkyl, or R1 and R3 together represent a 3- or 4-membered alkyl or alkenyl chain] are prepd. In an in vitro test for inhibitory effect on cGMP-PDE, cis-2,3,6,7,12,12a-hexahydro-2-(4-pyridylmethyl)-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione (prepn. given) showed IC50 of 10 nM.

IT 171488-69-0P 171488-89-4P 171488-90-7P

171489-00-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

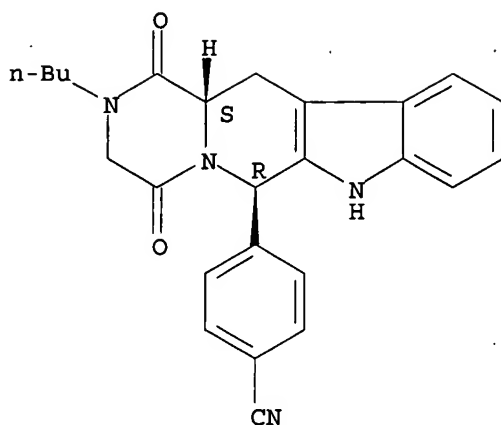
(prepn. of pyrazinopyridoindoliones as inhibitors of cyclic guanosine monophosphate specific phosphodiesterase)

RN 171488-69-0 CAPLUS

CN Benzonitrile, 4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxypyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

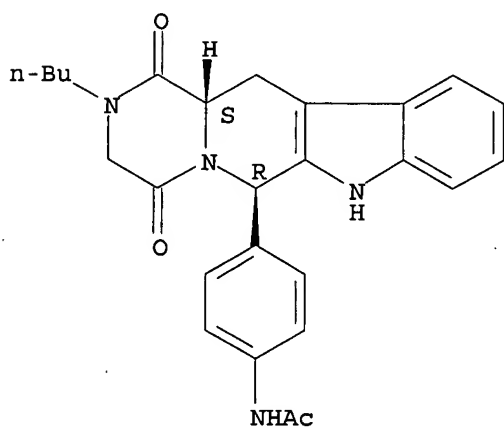
10/ 068,114



RN 171488-89-4 CAPLUS

CN Acetamide, N- [4- [(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

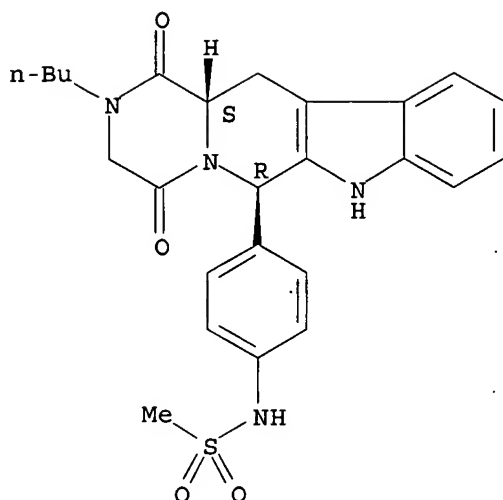


RN 171488-90-7 CAPLUS

CN Methanesulfonamide, N- [4- [(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

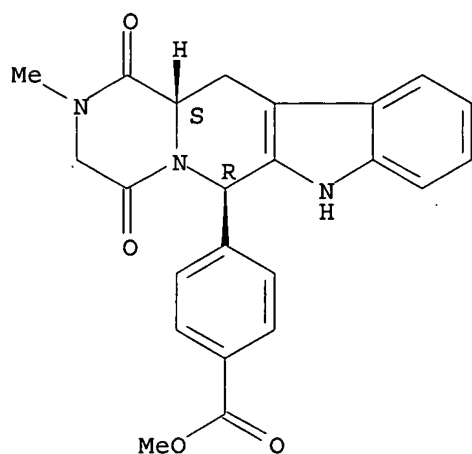
Relative stereochemistry.

10/ 068,114



RN 171489-00-2 CAPLUS
CN Benzoic acid, 4-(1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl)-, methyl ester, cis-(9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:516279 CAPLUS
DOCUMENT NUMBER: 111:116279
TITLE: Bicyclic piperidine compounds for use as stabilizers for organic materials
INVENTOR(S): Cantatore, Giuseppe; Borzatta, Valerio
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.; Ciba-Geigy S.p.A.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 294329	A2	19881207	EP 1988-810337	19880525
EP 294329	A3	19890726		
EP 294329	B1	19911113		
R: DE, FR, GB, IT				
US 4859724	A	19890822	US 1988-198269	19880525
CA 1299175	A1	19920421	CA 1988-568204	19880531
JP 63316780	A2	19881226	JP 1988-136629	19880602
JP 2613088	B2	19970521		

PRIORITY APPLN. INFO.:

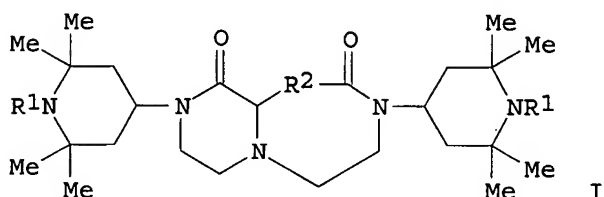
IT 1987-20750

19870602

OTHER SOURCE(S):

MARPAT 111:116279

GI



AB Stabilizers for org. materials, esp. synthetic polymers, are compds. having the formula I (R1 = H, O, OH, NO, CH2CN, C1-8 alkyl, allyl, benzyl, C1-8 acyl, OH-monosubstituted C2-4 alkyl, 2,3-epoxypropyl, C1-18 alkoxy, C5-12 cycloalkyloxy, 2,3-dihydroxypropyl; R2 = a direct bond or CH2). Refluxing 152.66 g N,N'-bis(2,2,6,6-tetramethyl-4-piperidyl)diethylenetriamine and 57.65 g di-Me fumarate in 150 mL trimethylbenzene for 4 h gave I (R1 = H, R2 = CH2) (II). A 50-.mu.m film made from a compn. of II 1, tris(2,4-di-tert-butylphenyl) phosphite 0.5, pentaerythritol tetrakis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate 0.5, Ca stearate 1, and polypropylene powder 1000 g had light stability 1920 h, compared with 380 h without II.

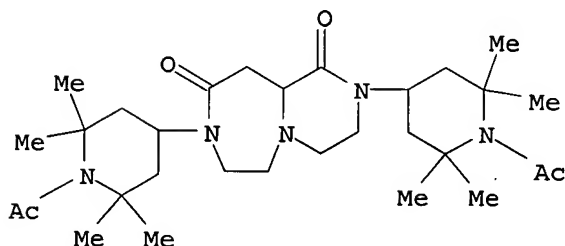
IT 121386-91-2

RL: USES (Uses)

(stabilizers, for synthetic polymers, prepn. and use of)

RN 121386-91-2 CAPLUS

CN Piperidine, 4,4'-(octahydro-1,9-dioxopyrazino[1,2-d][1,4]diazepine-2,8-diyl)bis[1-acetyl-2,2,6,6-tetramethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN.

ACCESSION NUMBER: 1988:528858 CAPLUS

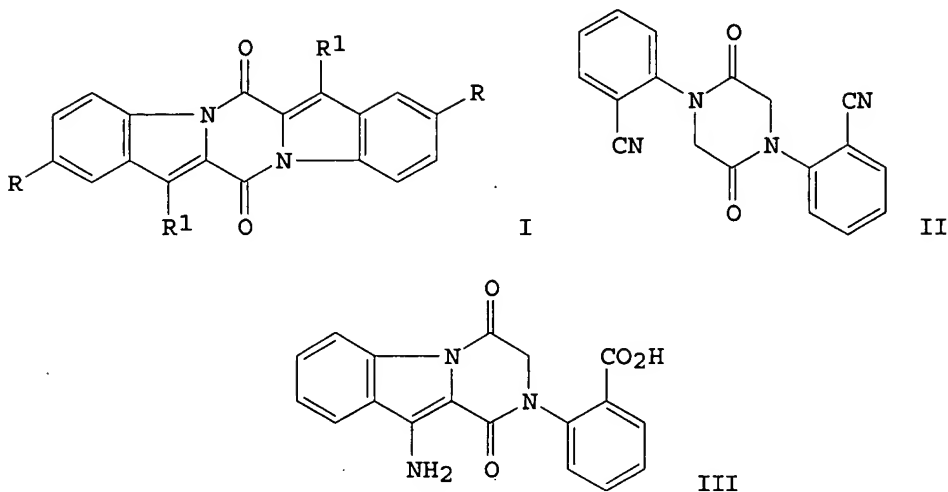
DOCUMENT NUMBER: 109:128858

TITLE: One-step synthesis of pyrazino(1,2-a:4,5-a')diindole-6,13-diones

AUTHOR(S): Schaefer, H.; Gewald, K.

CORPORATE SOURCE: Sekt. Chem., Tech. Univ. Dresden, Dresden, Ger. Dem. Rep.

SOURCE: Journal fuer Praktische Chemie (Leipzig) (1987),



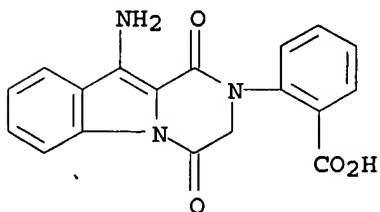
AB Thorpe Ziegler cyclization of 2-ClCH₂CONHC₆H₄CN in presence of NaOMe at 120.degree. gave 56% title compd. I (R = H, R₁ = NH₂). Some reaction of 20.degree. gave 69% 1,4-bis(o-cyanophenyl)piperazine-2,5-dione (II). Heating II at 120.degree. in NaOMe-DMF gave 70% I (R = H, R₁ = NH₂). Treatment of II with 4N NaOH gave 31% pyrazinoindole-1,4-dione III. Similar reaction of o-chloroacetamino ketone in NaOMe-DMF gave I (R = H, R₁ = Me; R = Cl, R₁ = Ph). Dieckmann reaction of N-chloroacetylanthranilic acid Et ester with NaH-DMF gave 38% I (R = H, R₁ = OH).

IT 116473-74-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of)

RN 116473-74-6 CAPLUS

CN Benzoic acid, 2-(10-amino-3,4-dihydro-1,4-dioxopyrazino[1,2-a]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1983:143372 CAPLUS

DOCUMENT NUMBER: 98:143372

TITLE: Attempted preparation of certain benzodiazepines

AUTHOR(S) : Abdel-Fattah, B.

CORPORATE SOURCE: Fac. Pharm., Univ. Cairo, Cairo, Egypt

10/ 068,114

SOURCE:

Pharmazie (1982), 37(9), 637-9

CODEN: PHARAT; ISSN: 0031-7144

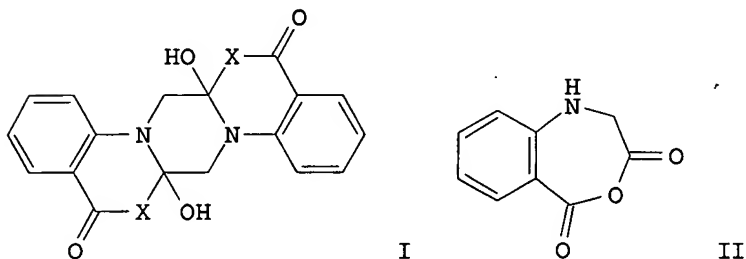
DOCUMENT TYPE:

Journal

LANGUAGE:

English

GI



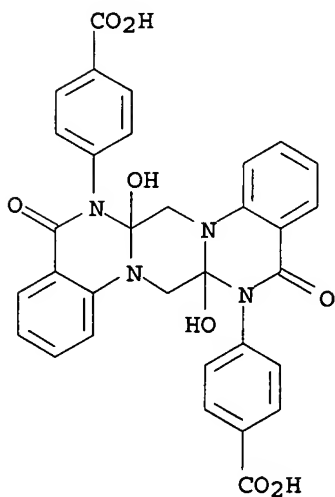
AB Cyclization of 2-HO₂CC₆H₄NHCH₂CO₂H with Ac₂O gave cyclodimer I (X = O), rather than the expected benzoxazepinedione II, a benzodiazepine intermediate. I (X = O) reacted with RNH₂ [R = (un)substituted Ph, naphthyl] to give 38-68% I (X = NR).

IT 84828-37-5P 84828-38-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

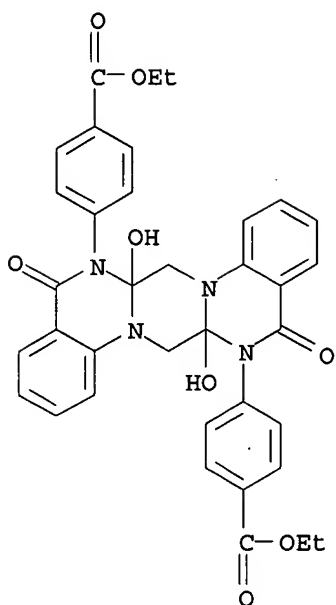
RN 84828-37-5 CAPLUS

CN Benzoic acid, 4,4'-(6a,7,14a,15-tetrahydro-6a,14a-dihydroxy-5,13-dioxopyrazino[1,2-a:4,5-a']diquinazoline-6,14(5H,13H)-diyl)bis- (9CI) (CA INDEX NAME)



RN 84828-38-6 CAPLUS

CN Benzoic acid, 4,4'-(6a,7,14a,15-tetrahydro-6a,14a-dihydroxy-5,13-dioxopyrazino[1,2-a:4,5-a']diquinazoline-6,14(5H,13H)-diyl)bis-, diethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1982:200709 CAPLUS
 DOCUMENT NUMBER: 96:200709
 TITLE: Thermostable composition
 INVENTOR(S): Chernikhov, A. Ya.; Yakovlev, M. N.; Rogov, N. S.
 PATENT ASSIGNEE(S): USSR
 SOURCE: Fr. Demande, 77 pp.
 CODEN: FRXXBL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2476068	A1	19810821	FR 1979-4447	19790221
FR 2476068	B1	19821203		

PRIORITY APPLN. INFO.: FR 1979-4447 19790221

AB Org. compds. which contain Si, halogen, N, S, P, B, and/or O atoms and contain NH₂, OH, SH, NCO, NSO, and/or NCS groups as well as cyano and/or ethynyl groups are mixed with a filler, such as TiO₂, MoS₂, Al, W, Co, Cu, graphite, glass fibers, asbestos, quartz, or silica, and polymd. to prep. apprxeq.110 heat-resistant resins which are esp. useful as binders (e.g., for abrasive particles such as diamonds and Si carbide) and adhesives. In some cases, the resins also contain a polyimide, polybenzoxazole, polyoxadiazole, polythioarylene, or similar resin which improves their mech. properties and heat resistance. Thus, 0.4 g powd. polybenzoxazole prepd. from bis(4-amino-3-hydroxyphenyl)methane and isophthalic acid was mixed with asbestos 0.8, 2,5-diamino-3,4-dicyanothiophene 0.24, and bis(4-isocyanatophenyl)methane 0.36 g and cured in a mold for 90, 90, and 30 min at 190, 250, and 300.degree., resp. The compressive strength (kg/cm²) of the molding was 1000 initially and 1150 after 500 h at 300.degree. in air.

IT 80905-41-5P

RL: PEP (Physical, engineering or chemical process); PREP (Preparation); PROC (Process)

(prepn. of heat-resistant, fillers for)

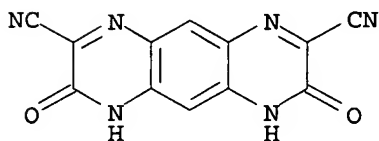
RN 80905-41-5 CAPLUS

10/ 068,114

CN Pyrazino[2,3-g]quinoxaline-2,8-dicarbonitrile, 3,4,6,7-tetrahydro-3,7-dioxo-, polymer with 3,5-diisocyanato-4-phenyl-4H-1,2,4-triazole (9CI)
(CA INDEX NAME)

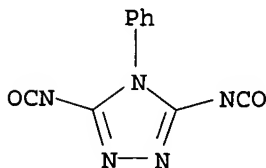
CM 1

CRN 75609-20-0
CMF C12 H4 N6 O2



CM 2

CRN 73461-00-4
CMF C10 H5 N5 O2



L4 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:640508 CAPLUS
DOCUMENT NUMBER: 93:240508
TITLE: Heat-resistant polymeric material
INVENTOR(S): Chernikhov, A. Ya.; Yakovlev, M. N.; Rogov, N. S.;
Petrova, A. P.; Martirosov, E. B.; Gul, V. E.
PATENT ASSIGNEE(S): USSR
SOURCE: Ger. Offen., 83 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2907195	A1	19800828	DE 1979-2907195	19790223
JP 55118914	A2	19800912	JP 1979-24370	19790302
JP 60021647	B4	19850529		
US 4458041	A	19840703	US 1980-199116	19801017
PRIORITY APPLN. INFO.:			US 1979-8562	19790201
			DE 1979-2907195	19790223

AB Monomers (and, in some cases, low-mol.-wt. polymers) contg. NH₂, OH, SH, NCO, NSO, and/or NCS groups as well as cyano and/or ethynyl groups are polymd. to prep. .apprx.110 polymers which are resistant to degrdn. at 300-400.degree.. In most cases, the monomers and low-mol.-wt. polymers are mixed with fillers such as TiO₂, powd. metals, glass fibers, carbon fibers, graphite, powd. polyoxadiazole, polybenzoxazole, polyimide, or fluoropolymer, asbestos, MoS₂, BN, silica, diamond dust, and/or SiC. The heat-resistant polymeric materials are useful as moldings, adhesives,

10/ 068,114

grinding disks, etc. Thus, a mixt. of bis(3-amino-4-cyanophenyl) ether 0.16, bis(4-isocyanatophenyl)methane 0.16, graphite 0.2, and a powd. poly-1,3,4-oxadiazole 0.78 g was molded at 130-200.degree./245 bars, demolded, and heated at 300.degree. for 30 min to prep. a molding which had compressive strength (MN/m2) 96 initially and 108 after 500 h in air at 300.degree. and had flexural strength (MN/m2) 31 initially and 35 after heat aging.

IT 75659-00-6P

RL: PEP (Physical, engineering or chemical process); PREP (Preparation); PROC (Process)

(manuf. of heat-resistant, filler-contg.)

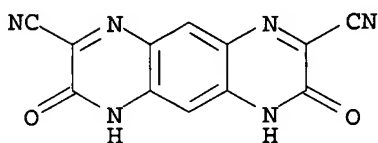
RN 75659-00-6 CAPLUS

CN Pyrazino[2,3-g]quinoxaline-2,8-dicarbonitrile, 3,4,6,7-tetrahydro-3,7-dioxo-, polymer with 3,5-diisocyanato-4-phenyl-4H-1,2,4-triazole and 1,2-diphenyl-1,2-dicarbododecaborane(12) (9CI) (CA INDEX NAME)

CM 1

CRN 75609-20-0

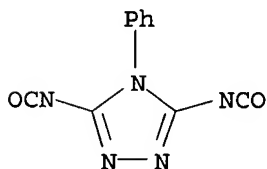
CMF C12 H4 N6 O2



CM 2

CRN 73461-00-4

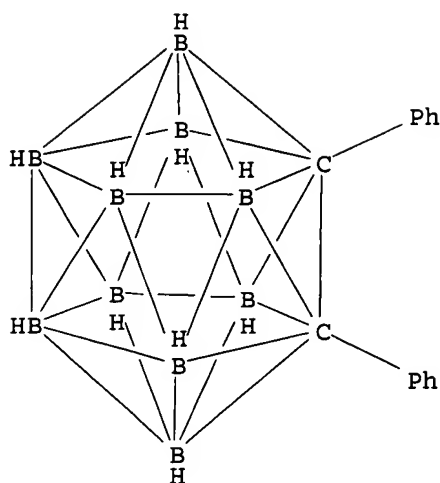
CMF C10 H5 N5 O2



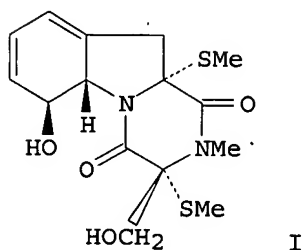
CM 3

CRN 17805-19-5

CMF C14 H20 B10

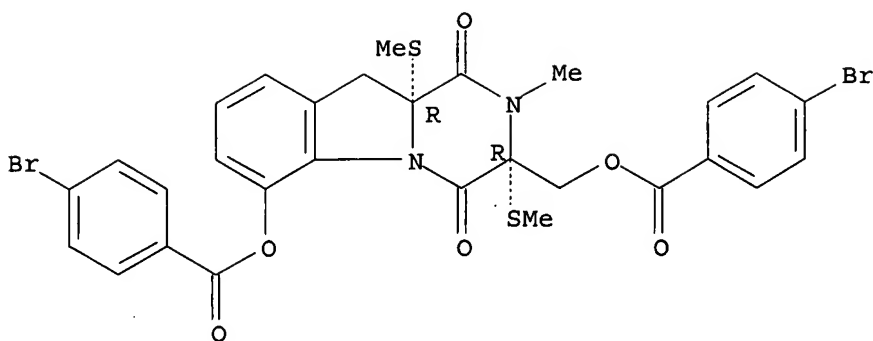


L4 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1980:446585 CAPLUS
 DOCUMENT NUMBER: 93:46585
 TITLE: Biosynthesis of bisdethiobis(methylthio)gliotoxin, a new metabolite of *Gliocladium deliquescens*
 AUTHOR(S): Kirby, Gordon W.; Robins, David J.; Sefton, Mark A.; Talekar, Ratnaker R.
 CORPORATE SOURCE: Dep. Chem., Univ. Glasgow, Glasgow, G12 8QQ, UK
 SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1980), (1), 119-21
 CODEN: JCPRB4; ISSN: 0300-922X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI

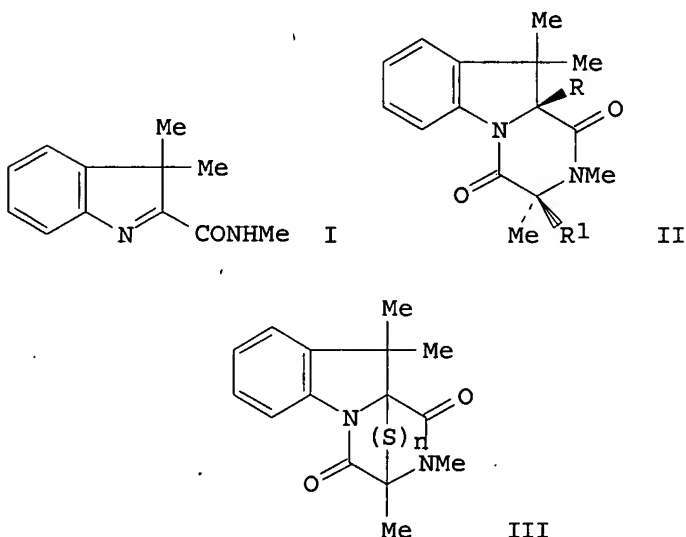


AB The title compd. (I), isolated from *G. deliquescens*, was identified by chem. and spectral methods. Feeding expts. showed that I is formed in *G. deliquescens* by irreversible redn. and methylation of gliotoxin.
 IT 74181-99-0P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
 RN 74181-99-0 CAPLUS
 CN Benzoic acid, 4-bromo-, [6-[(4-bromobenzoyl)oxy]-1,2,3,4,10,10a-hexahydro-2-methyl-3,10a-bis(methylthio)-1,4-dioxopyrazino[1,2-a]indol-3-yl]methyl ester, (3R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1976:560025 CAPLUS
 DOCUMENT NUMBER: 85:160025
 TITLE: Approaches to analogs of dehydrogliotoxin. 6. An efficient synthesis of a gliotoxin analog with anti-reverse transcriptase activity
 AUTHOR(S): Ottenheijm, Henricus C. J.; Herscheid, Jacobus D. M.; Kerkhoff, Gerardus P. C.; Spande, Tom F.
 CORPORATE SOURCE: Dep. Org. Chem., Cathol. Univ. Nijmegen, Nijmegen, Neth.
 SOURCE: Journal of Organic Chemistry (1976), 41(21), 3433-8
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB The addn. of $\text{MeCOCOC}\text{Cl}$ to the indolenine-2-carboxamide I followed by spontaneous, diastereoselective ring closure to 3,6-disubstituted dioxopiperazines II ($\text{R} = \text{Cl}$, $\text{R}_1 = \text{OH}$) provides an efficient, new synthesis of gliotoxin analogs. II ($\text{R} = \text{Cl}$, $\text{R}_1 = \text{OH}$) was converted into the mercaptoalkene by treatment with H_2S . Regiospecific and diastereoselective addn. of H_2S to the exo methylene group gave II ($\text{R} = \text{R}_1 = \text{HS}$). Several oxidn. procedures were studied for the conversion of II ($\text{R} = \text{R}_1 = \text{HS}$) into disulfide III ($n = 2$). III ($n = 2,3$) were obtained from II ($\text{R} = \text{R}_1 = \text{HS}$) by reaction with SCl_2 and S_2Cl_2 , resp.; the monosulfide

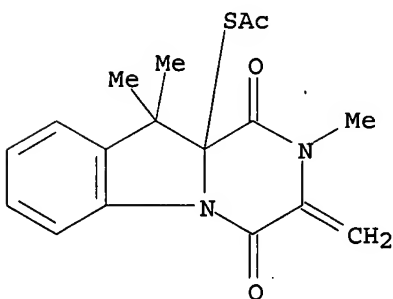
III (n = 1) was prepd. from III (n = 2) by treatment with Ph₃P. Analogs between this synthesis and what is known about the biosynthesis of gliotoxin are discussed. III (n = 2) (81% overall yield) inhibits the enzyme reverse transcriptase, while having no effect on transcriptase; its activity is comparable to that of gliotoxin.

IT 59888-46-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 59888-46-9 CAPLUS

CN Ethanethioic acid, S-(1,2,3,4-tetrahydro-2,10,10-trimethyl-3-methylene-1,4-dioxopyrazino[1,2-a]indol-10a(10H)-yl) ester (9CI) (CA INDEX NAME)



L4 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1976:43989 CAPLUS

DOCUMENT NUMBER: 84:43989

TITLE: Three-step synthesis of a gliotoxin analog with antireverse transcriptase activity

AUTHOR(S): Ottenheijm, Henricus C. J.; Kerkhoff, Gerardus P. C.;
Bijen, Johannes W. H. A.; Spande, Tom F.

CORPORATE SOURCE: Dep. Org. Chem., Univ. Nijmegen, Nijmegen, Neth.

SOURCE: Journal of the Chemical Society, Chemical
Communications (1975), (19), 768-9

CODEN: JCCCAT; ISSN: 0022-4936

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

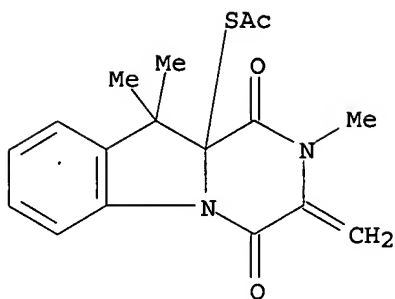
AB A method of general applicability to the prepn. of analogs of gliotoxin involved addn. of Me(CO)₂Cl to the carboxamide I, prepd. by condensation of Et 3,3-dimethylindolenine-2-carboxylate and MeNH₂, followed by cyclization of the Leuchs' adduct formed to give II (R = Cl, R₁ = OH). Treatment of II (R = Cl, R₁ = OH) with H₂S-ZnCl₂ at 0.degree. gave the cis-dithiol II (R = R₁ = SH) which underwent oxidn. to give 37% disulfide III (n = 2) and thionation to give III (n = 4). Treatment of III (n = 2) with PPh₃ in EtOH gave 20% III (n = 1). III (n = 2) inhibited reverse transcriptase, the RNA-dependent DNA polymerases of RNA tumor viruses.

IT 59888-46-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 59888-46-9 CAPLUS

CN Ethanethioic acid, S-(1,2,3,4-tetrahydro-2,10,10-trimethyl-3-methylene-1,4-dioxopyrazino[1,2-a]indol-10a(10H)-yl) ester (9CI) (CA INDEX NAME)



L4 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1975:578991 CAPLUS

DOCUMENT NUMBER: 83:178991

TITLE: Convenient synthesis of dioxopiperazines via

aminolysis of .alpha.-(pyruvylamino) esters

AUTHOR(S): Marshall, J. A.; Schlaf, T. F.; Csernansky, J. G.

CORPORATE SOURCE: Dep. Chem., Northwest. Univ., Evanston, IL, USA

SOURCE: Synthetic Communications (1975), 5(3), 237-44

CODEN: SYNCAV; ISSN: 0039-7911

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

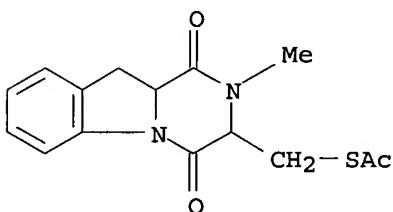
AB Dioxopiperazines I and II were prepd. from indoline III by cyclizing with MeNH2 to give dioxopiperazine IV, which was dehydrated to methylene compd. V. V added AcSH to give I and II. Analogous reactions starting with pyrrole VI gave dioxopiperazine VII.

IT 57101-32-3P 57101-33-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

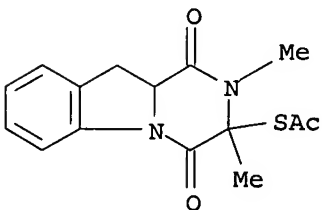
RN 57101-32-3 CAPLUS

CN Ethanethioic acid, S-[(1,2,3,4,10,10a-hexahydro-2-methyl-1,4-dioxopyrazino[1,2-a]indol-3-yl)methyl] ester (9CI) (CA INDEX NAME)

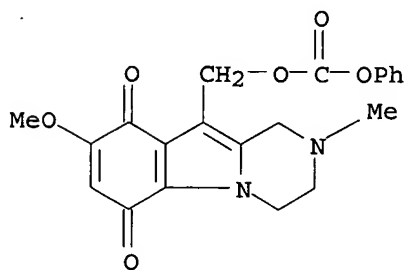


RN 57101-33-4 CAPLUS

CN Ethanethioic acid, S-(1,2,3,4,10,10a-hexahydro-2,3-dimethyl-1,4-dioxopyrazino[1,2-a]indol-3-yl) ester (9CI) (CA INDEX NAME)



L4 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1972:113169 CAPLUS
 DOCUMENT NUMBER: 76:113169
 TITLE: Synthesis of mitomycin analogs. I. Synthesis of
 2-methylpiperazino[1,2-a]indole-6,9-diones
 AUTHOR(S): Yamada, Yasuhiro; Takai, Haruki; Hatano, Kota;
 Sakakibara, Masayuki; Matsui, Masanao
 CORPORATE SOURCE: Dep. Agric. Chem., Univ. Tokyo, Tokyo, Japan
 SOURCE: Agricultural and Biological Chemistry (1972), 36(1),
 106-11
 CODEN: ABCHA6; ISSN: 0002-1369
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB Alkylation of the indolecarboxylate (I) with Et bromoacetate and NaH in
 THF, followed by reaction with MeNH₂ and heating, gave a dione (II).
 Redn. of II, followed by formylation, yielded the aldehyde (III).
 Nitration of III followed by redn. gave the aminoaldehyde (IV). Oxidn. of
 IV followed by redn. gave a hydroquinone, which on oxidn. gave the
 2-methylpiperazino[1,2-a]-indole-6,9-dione (V, R₁ = H, R₂ = OMe), from
 which were prepd. V (R₁ = CONH₂, CONHMe; R₂ = NH₂, OMe). V (R₁ = CONH₂,
 R₂ = OMe), e.g., was effective in vitro against, e.g., Staphylococcus
 aureus at min. inhibitory concn. 0.19 .mu.g/ml.
 IT 35727-35-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)
 RN 35727-35-6 CAPLUS
 CN Carbonic acid, (1,2,3,4,6,9-hexahydro-8-methoxy-2-methyl-6,9-
 dioxopyrazino[1,2-a]indol-10-yl)methyl phenyl ester (9CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 07:51:19 ON 11 SEP 2003)

FILE 'REGISTRY' ENTERED AT 07:51:28 ON 11 SEP 2003

L1 STRUCTURE UPLOADED
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 L3 56 S 'DIOXO PYRAZINO'

FILE 'CAPLUS' ENTERED AT 07:53:17 ON 11 SEP 2003

L4 24 S L3

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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